



# Coronary Artery Z-scores in Febrile Children with Suspected Kawasaki's Disease—The Value of Serial Echocardiography

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## Abstract

**Background** Progressive enlargement of the coronary artery (CA) diameters on serial echocardiography can support diagnosis of Kawasaki's disease (KD) even CA dimensions are within the normal range.

**Methods** A single-center, retrospective study compared mean Z-scores of the proximal CA internal diameters in children hospitalized with non-KD febrile illnesses (FCs) with those of KD patients.

**Results** A total of 223 patients with suspicion of KD have been admitted over a period of 16 years and data were evaluable for 176 children. Distributions for age, sex, and body surface area were similar for both groups. FC had a significantly shorter duration of hospitalization, higher levels of hemoglobin, lower levels of liver transaminases, and segmented neutrophils, respectively. The majority of FC patients (75/82, 91.5%) had normal CA Z-scores ( $p < 0.001$ ) and only 3 (3.7%) had CA Z-score  $\geq 2.5$  standard deviation (SD). In KD, subjects (46/94, 49.5%) had a CA dilation (Z-score  $\geq 2.5$  SD) and the maximum CA Z-score (Zmax) was significantly higher compared with FC patients ( $p < 0.001$ ). On serial echocardiograms, FC patients showed a mild decrease, whereas KD patients developed a significant increase of CA Zmax ( $p < 0.001$ ). Seven KD patients had a segmental dilation of a CA which has been confirmed by cardiac catheter. In FC, no segmental dilation of any CA was documented by echocardiography.

**Conclusion** This study found that mean CA dimensions in FCs were smaller and did not increase in serial echocardiograms compared with KD patients.

## Keywords

- ▶ Kawasaki's disease
- ▶ aneurysm
- ▶ coronary artery
- ▶ serial echocardiography
- ▶ Z-scores
- ▶ febrile children

## Introduction

Kawasaki's disease (KD) is an acute vasculitis of unknown etiology affecting small- and medium-sized arteries of all body regions, especially in children younger than 5 years of age. Up to 25% of untreated patients suffer from coronary artery (CA) abnormalities with increased short- and long-

term morbidity and mortality.<sup>1,2</sup> The diagnosis is made in the presence of fever of 5 days or more combined with four of the five clinical criteria. With fewer than four criteria present, the diagnosis of incomplete KD should be considered. In these patients, diagnosing KD is even more challenging particularly as there is a higher risk of cardiac complications.<sup>3,4</sup> Therefore, the American Heart Association (AHA)

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recommends performing basis echocardiography as soon as KD is considered.<sup>5</sup> Delayed KD diagnosis and treatment after day 10 of fever are reported risk factors in developing CA aneurysms.<sup>6-8</sup> In recent times, Z-scores have been used to evaluate CA lesions in patients with KD. The Z-score is an index of CA dimensions that is standardized to sex and body surface area (BSA). Therefore, the Z-score may be useful for direct and sensitive detection of early CA dilatation compared with clinical findings.<sup>9</sup> Normative measurements of CA Z-scores are based on assessment of healthy afebrile children.<sup>5</sup> Fuse et al reported that 23.4% of KD patients show CA dilation (Z-score  $\geq 2.0$  standard deviation [SD]) after day 5 and 70% after day 10 of illness.<sup>10</sup> However, there is an uncertainty about the specificity of arterial dilation in KD and the possibility has been raised that febrile children illnesses other than KD (FC) can also cause CA dilation.<sup>11</sup> Of note, CA enlargement has been reported in patients with other inflammatory, genetic, and infectious diseases.<sup>12</sup> Very recently, it has been shown that serial echocardiograms were helpful to diagnose and treat incomplete KD early to prevent CA lesions.<sup>13</sup> To determine whether dilation of the proximal CA can occur in FC, we assessed luminal dimensions normalized for BSA as Z-scores and compared serial measurements with those of KD patients.

## Methods

### Study Population

The retrospective analyzed data were collected from clinical records of patients treated at the children's university hospital Regensburg (KUNO, Clinic St. Hedwig). We included all infants and children with suspected KD admitted to our hospital between March 2002 and May 2018. Demographic data and records on medical, personal, and family history were obtained. Laboratory tests were performed according to the hospital's standard procedures. BSA was calculated using the formula of Haycock et al.<sup>14</sup> We defined the first reported day of fever as first day of illness. Our patients were classified according to the AHA guidelines.<sup>5</sup> Patients with a history of vascular or cardiovascular disease, congenital heart defect, systemic hypertension, weight for height  $>95$ th percentile or  $<5$ th percentile, family history of hypertrophic or dilated cardiomyopathy, rheumatologic disorders, a history of vasculitis, or KD were excluded from our study. Except for two children with Asian ancestry, all participants of this study were of Caucasian descent.

The study is in compliance with the Declaration of Helsinki and was approved by the Institutional Review Board of the University of Regensburg (file number 14-101-0206).

### Echocardiography

If there was a suspicion for KD, a cardiological evaluation including a 12-lead electrocardiogram and an initial (P1) transthoracic echocardiography (TTE) was performed. Serial TTE (P2) were conducted if diagnosis could not be established with clinical findings, laboratory tests, and initial echocardiography. As multiple echocardiograms were performed in P2, we used the highest Z-score (P2 Z<sub>max</sub>) of a CA segment for analysis. Two-dimensional, M-mode, Doppler

and color Doppler echocardiography was performed (Aplio 500 CV; Toshiba Medical Systems Corporation, Otawara, Japan) with a 6.5, 5.0, or 3.0 MHz transducer (PST65-BT, PST-50BT, PST-30BT; Toshiba). All subjects were examined in supine or left lateral decubitus position by well-experienced pediatric cardiologists. S.G. was responsible for 87% and H.M. for 13% of the analyzed echocardiograms.

In accordance with the AHA scientific statement on KD,<sup>5</sup> the proximal coronary arteries were examined in the parasternal short or long axis view. As they advise, measurements of the left main CA should be viewed with caution because of anatomic variations such as a dominant left or right CA system. The distance from the trailing edge of the near wall to the leading edge of the far wall was measured as the internal CA diameter 5 mm distal the ostium.<sup>10</sup> If there was a short stem of the left CA (LCA) ( $<5$  mm), the diameter was measured in the middle between the ostia and the branching. For statistical interpretation, we used averaged values from two or three single measurements of the CA luminal diameter.

To diagnose CA involvement by using echocardiography, we assessed luminal dimensions normalized for BSA as Z-scores according to Dallaire et al.<sup>15</sup> The highest Z-score of the main right (RCA), main LCA, left anterior descending (LAD), and left circumflex (LCX) CAs was expressed as Z<sub>max</sub> at each phase.

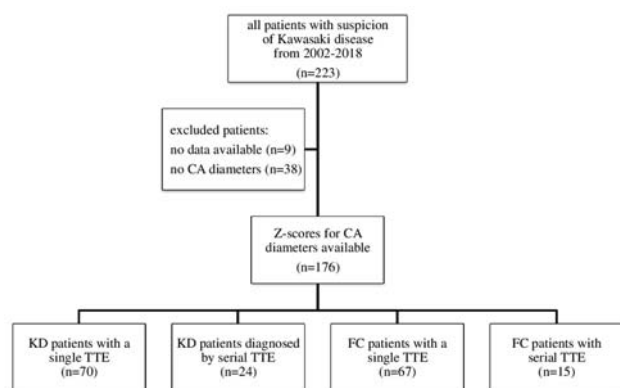
A mean Z-score  $<2.0$  SD was determined as normal, whereas a mean Z-score between 2.0 and  $<2.5$  SD was declared as dilation. Small aneurysm of a CA was defined as a mean Z-score 2.5 to  $<5.0$ , medium aneurysm 5.0 to  $<10$ , and large aneurysm from  $\geq 10$  or absolute dimension  $\geq 8$  mm.<sup>15</sup> All studies were digitally stored for off-line analysis, retrospective re-evaluation, and follow-up examinations.

### Statistics

Demographic and epidemiological characteristics are presented using absolute and relative frequencies for categorical variables and median (quartile 1, quartile 3) for continuous data. Comparisons between KD and FC patients were performed using a chi-square test of independence or the Mann-Whitney's *U*-test, respectively. For the analysis of changes in Z-scores of coronary arteries, paired Student's *t*-tests were applied. Z-score categories were compared between patients with KD and FC using the chi-square test of independence. A *p*-value of  $<0.05$  was considered statistically significant. Statistical analysis was performed using IBM SPSS Statistics 25 software.

## Results

During the study period, 223 patients with suspicion of KD had been admitted to our hospital. One hundred twenty-four patients were diagnosed suffering from KD and 99 patients had febrile illnesses other than KD. Nine of them were excluded because of missing clinical reports and 38 patients because of incomplete echocardiographic results, leaving a total of 176 children for analysis ( $\rightarrow$  Fig. 1). Clinical and epidemiological data of 82 FC and 94 KD patients are shown in  $\rightarrow$  Table 1. Within 24 hours before echocardiography, the maximum body temperatures were 40°C (39.3; 40.3) and 40°



**Fig. 1** Flow chart of 223 patients with suspicion of KD. In 176 patients, Z-scores for internal CA diameters were available for analysis. CA, coronary artery; FC, children with febrile illnesses other than KD; KD, Kawasaki's disease; TTE, transthoracic echocardiography; Z-scores, standard deviation units from the mean.

C (39.6; 40.5) for the FC and KD subjects, respectively. In average, patients were diagnosed having KD after a median of day 6 of illness (range: 1–26 days), and 81 patients (86%) were diagnosed within the first 10 days of fever.

The diagnosis for the 82 analyzed FC was acute infectious diseases as follows: viral upper respiratory illness ( $n = 29$ ), self-limited febrile illness without specific diagnosis ( $n = 26$ ), pneumonia ( $n = 6$ ), viral gastroenteritis ( $n = 5$ ), pyelonephritis ( $n = 3$ ), stomatitis ( $n = 3$ ), urinary tract infection ( $n = 3$ ), bronchiolitis ( $n = 2$ ), Epstein–Barr virus infection ( $n = 2$ ), appendicitis ( $n = 1$ ), purulent otitis media, ( $n = 1$ ), and osteomyelitis ( $n = 1$ ). None of these patients received an immunomodulatory treatment. The median duration of fever at the time of the echocardiography was 6 days (range: 2–15).

## Echocardiographic Data

In our cohort, diagnosis of complete KD was made before echocardiography in 7 of 176 patients (7.5%). These patients showed typical clinical features and laboratory test results. In 63 patients (67%), KD was diagnosed on the day of their initial echocardiography (P1) that was performed on the seventh day of fever (mean, range: 1–26 days).

The maximum CA Z-score ( $Z_{max}$ ) was significantly higher for the KD subjects compared with FC (– **Table 2**). Of the 63 subjects suffering from a complete KD, 22 patients (35%) had maximum Z-scores from 2.5 to  $< 5.0$  SD, and five patients (8%) had a  $Z_{max}$  above 5.0 SD. In patients with an incomplete KD, these findings were even more pronounced. Of 31 patients with incomplete KD, 16 patients (51.6%) had at least one maximum CA Z-score of 2.5 to  $< 5.0$  SD, and 3 patients (9.7%) had  $Z_{max}$  above 5.0 SD. Overall, 46 (49.5%) KD subjects had a  $Z_{max} \geq 2.5$  SD.

Of all KD patients, seven subjects developed a segmental dilation of a CA. The invasive angiography showed that five patients with complete KD suffered from an aneurysm in the LCA ( $n = 2$ ) or RCA ( $n = 3$ ), one patient with complete KD developed two aneurysms in both main coronary arteries, and one female with incomplete KD had aneurysms in the LCA, LAD, and RCA, respectively.

In contrast, the majority of FC patients (75/82, 91.5%) had CA Z-scores  $< 2.0$  SD. Four patients (4.9%) had a  $Z_{max}$  between 2.0 and  $< 2.5$  SD with diagnosis of viral upper respiratory illness, pneumonia, nephritis, and septic disease, respectively. Only 3 of 82 patients (3.7%) had a maximum CA Z-score from 2.5 to  $< 5.0$  SD ( $p < 0.001$ ). The first was a 1-year-old girl with viral hepatitis (RCA- $Z_{max}$  2.6 SD). Six days later, the RCA dimension had normalized. The second was a 6-year-old girl with polyserositis presenting with a dominant left coronary

**Table 1** Clinical and epidemiological data of 82 FC patients, 63 patients with complete KD, and 31 patients with incomplete KD

Variable	FC ( $n = 82$ )	Complete KD ( $n = 63$ )	Incomplete KD ( $n = 31$ )	$p$ -Value
Male, $n$ (%)	43 (52%)	45 (71%)	18 (58%)	0.066
Age, mo	43 (26; 69)	40 (27; 67)	50 (13; 92)	0.992
BSA, $m^2$	0.67 (0.55; 0.77)	0.64 (0.55; 0.80)	0.63 (0.49; 0.89)	0.907
Maximum body temperature, $^{\circ}C$	40 (39.3; 40.3)	40 (39.7; 40.2)	40 (39.6; 40.5)	0.236
Duration of hospitalization, d	4 (3; 6)	7 (6; 9)	7 (6; 10)	$< 0.001$
CRP, mg/dL	61.4 (15.8; 133.0)	90 (52; 169)	100 (55.3; 193.0)	0.026
Hb, g/dL	11.2 (10.5; 12)	10.4 (9.5; 11.2)	10.1 (9.0; 11.3)	$< 0.001$
WBC count, $10^9/L$	12.6 (8.3; 18.2)	14.1 (11.8; 19.6)	16.7 (10.7; 19.8)	0.029
Segmented neutrophils, %	59 (48; 68)	70 (60; 76)	60 (53; 72)	0.001
Platelet count, $10^{10}/L$	34.1 (26.6; 42.3)	56.9 (47.9; 76.9)	61.7 (33.4; 77.2)	$< 0.001$
Sodium, mmol/L	133 (131; 135)	131 (128; 134)	131 (130; 134)	0.002
AST, U/L	34 (27; 43)	43 (31; 75)	42 (34; 52)	0.007
ALT, U/L	14 (11; 26)	49 (20; 114)	21 (15; 42)	$< 0.001$
$\gamma$ -GT, U/L	14 (9; 23)	42 (17; 96)	22 (11; 83)	$< 0.001$

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BSA, body surface area; CRP, C-reactive protein; FC, children with febrile illnesses other than KD;  $\gamma$ -GT, gammaglutamyl transferase; Hb, hemoglobin; KD, Kawasaki's disease; WBC, white blood cell.

Notes: Data are expressed in median and interquartile range. Data are expressed in median (quartile 1; quartile 3), maximum values of CRP, WBC, segmented neutrophils, platelets, AST, ALT,  $\gamma$ -GT, and minimum values of Hb and sodium of all laboratory results. For statistical analysis, complete and incomplete KD patients were grouped together. A  $p$ -value of  $< 0.05$  was considered statistically significant.

**Table 2** Coronary artery Z-score results of basic echocardiography

Zmax	FC (n = 82)	Complete KD (n = 63)	Incomplete KD (n = 31)	p-Value
< 2.0 SD	75 (91.5%)	22 (35%)	8 (25.8%)	<0.001
2.0–< 2.5 SD	4 (4.9%)	14 (22%)	4 (12.9%)	
2.5–< 5.0 SD	3 (3.7%)	22 (35%)	16 (51.6%)	
≥ 5.0 SD	0	5 (8%)	3 (9.7%)	

Abbreviations: FC, children with febrile illnesses other than KD; KD, Kawasaki's disease; Zmax, maximum Z-score results of 63 patients with complete, 31 patients with incomplete KD, and 82 FC patients with available measurements for the proximal coronary arteries.

Notes: Statistical analysis by chi-square-test. For statistical analysis, complete and incomplete KD patients were grouped together. A p-value of < 0.05 was considered statistically significant.

**Table 3** Results of serial echocardiography in 19 KD patients

	Zmax P1	Zmax P2	Δ Zmax	p-Value
LCA (n = 19)	0.72 ± 1.13	+1.65 ± 1.22	+0.93 (95% CI: 0.52, 1.33)	<0.001
RCA (n = 15)	−0.03 ± 1.25	+0.94 ± 1.12	+0.97 (95% CI: 0.33, 1.61)	0.006
LAD (n = 9)	0.49 ± 1.04	+1.69 ± 0.53	+1.20 (95% CI: 0.32, 2.08)	0.014
LCX (n = 3)	−0.16 ± 1.39	+0.54 ± 1.42	+0.70 (95% CI: −0.18, 1.58)	0.076

Abbreviations: CI, confidence interval; Δ Zmax, difference between Zmax P1 and Zmax P2 (95% CI); KD, Kawasaki's disease; LAD, left anterior descending; LCA, left coronary artery; LCX, left circumflex; RCA, right coronary artery; Zmax P1, highest Z-score in initial echocardiography; Zmax P2, highest Z-score in multiple echocardiographies before treatment.

Note: A p-value of < 0.05 was considered statistically significant.

system and a short main stem of the LCA with a Zmax of 3.7 SD (LCA 3.1 mm). The internal LCA diameter of 3.1 mm did not decrease on serial echocardiograms. The third was an 11-year-old boy with pneumonia and a LAD Zmax of 3.1 SD (LAD 3.0 mm). Four weeks later, the LAD diameter decreased to a Z-score of 2.1 SD. No FC patient had a Zmax above 5.0 SD, and there was no segmental dilation of any CA on echocardiography. After demission from our hospital, none of the FC cohort showed up with periungual desquamation of the skin, Beau's lines, or cardiologic symptoms in our outpatient clinic.

### Serial Echocardiography

We performed serial measurements (P2) of the CA diameters if diagnosis of KD could not be established with clinical symptoms, laboratory results, and initial echocardiography (P1). So, in 24/94 children (26%), multiple TTEs with two or more examinations were necessary to confirm diagnosis of KD (►Table 3). Most of these patients (16/24, 83%) underwent echocardiography two times. In 3/24 patients (16%), three TTEs were performed, and in 1/24 patient, four TTEs were necessary to diagnose KD. Mean interval between P1 and P2 was 1.8 days, with a minimum of 1 and a maximum of 4 days.

Data for CA Z-scores were available in 19/24 (79%) of KD patients. Mean maximum CA Z-scores (Zmax) for the LCA (n = 19) increased significantly between P1 and P2 (p < 0.001). Mean CA Zmax for the RCA (n = 15) also increased significantly between P1 and P2 (p = 0.008). The LAD Z-scores were available for nine patients, eight of them showed an increase of the Z-score and in one patient, the LAD diameter did not change (p = 0.014). For LCX, CA Z-scores were available just for three patients and all of these patients showed an increase in Z-score (p = 0.076). When enlargement of the CA diameter was detected, diagnosis of

KD was considered most likely, and therapy was initiated. It is noticeable that patients with greater intervals between P1 and P2 (3 or more days) showed a greater increase of CA Z-scores, but a significant increase in CA internal diameters could already be identified after an interval of 24 hours.

In 15/82 FC patients (18%), results of serial echocardiography were available for all four proximal CA segments. With a mean of 1.7 days, the interval between P1 and P2 in FC was comparable to the KD cohort (minimum of 1 day and maximum of 4 days). Every patient of this FC subgroup showed a mild decrease of CA internal diameters (Δ Zmax) (►Table 4).

We would like to emphasize that serial echocardiography in febrile children, suspected to have KD, helps improve diagnosis, as CA dimension in KD patients increase and in FC patients not (►Fig. 2).

### Discussion

We analyzed the mean CA dimensions of hospitalized children with suspected KD by echocardiography. KD patients had significantly higher maximum Z-scores (Zmax) and showed a significant increase of CA internal diameters by serial echocardiograms compared with FC. In addition, only one-third of all KD patients measured normal CA dimensions, while the vast majority (91.5%) of FC patients were within normal limits. Moreover, nearly half of the KD subjects of our cohort had a CA Zmax ≥ 2.5 SD and seven patients developed a segmental dilation of a CA confirmed by invasive angiography. In the FC group, transient CA dilation was found in a child with viral hepatitis (RCA Zmax 2.6 SD) and in another patient with bacterial pneumonia with a decrease of LAD Zmax from 3.1 to 2.1 SD on re-evaluation after 4 weeks. One FC patient demonstrated

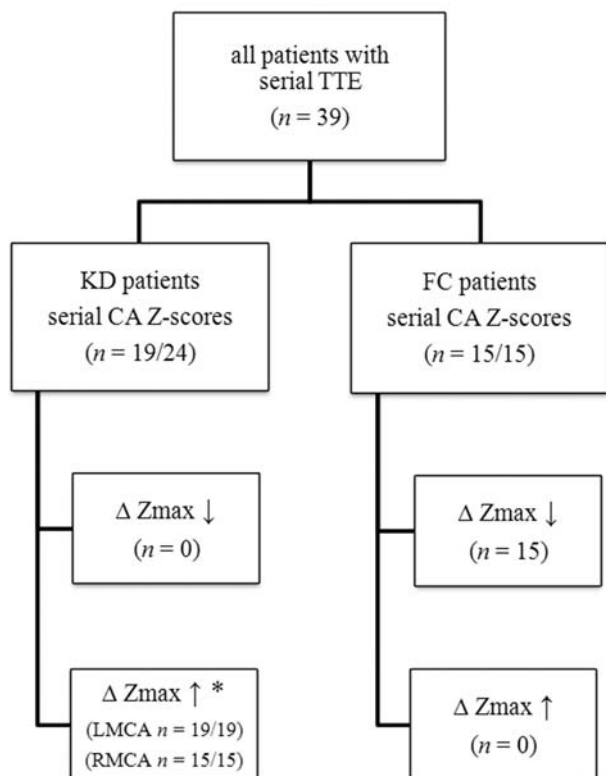


**Table 4** Results of serial echocardiography in 15 FC with illnesses other than KD

	Zmax P1	Zmax P2	$\Delta$ Zmax	p-Value
LCA (n = 15)	0.43 $\pm$ 0.98	0.12 $\pm$ 1.02	-0.31 (95% CI: -0.69, 0.06)	0.097
RCA (n = 15)	-0.15 $\pm$ 0.71	-0.61 $\pm$ 1.33	-0.46 (95% CI: -0.95, 0.04)	0.068
LAD (n = 15)	-0.05 $\pm$ 0.81	-0.32 $\pm$ 0.82	-0.28 (95% CI: -0.60, 0.04)	0.090
LCX (n = 15)	-0.91 $\pm$ 0.85	-0.95 $\pm$ 0.88	-0.04 (95% CI: -0.30, 0.23)	0.778

Abbreviations: CI, confidence interval;  $\Delta$  Zmax, difference between Zmax P1 and Zmax P2 (95% CI); FC, children with febrile illnesses other than KD; KD, Kawasaki's disease; LAD, left anterior descending; LCA, left coronary artery; LCX, left circumflex; RCA, right coronary artery; Zmax P1, highest Z-score in initial echocardiography; Zmax P2, highest Z-score in multiple echocardiographies before treatment.

Note: A p-value of < 0.05 was considered statistically significant.



**Fig. 2** Flow chart of 39 patients with serial TTE. In 19/24 KD patients and in 15 FC, serial Z-scores for internal CA diameters were available for analysis. CA, coronary artery;  $\Delta$  Zmax, difference between highest initial CA Z-score and highest CA Z-score in multiple TTE before treatment; FC, children with febrile illnesses other than KD; KD, Kawasaki's disease; LMCA, left main coronary artery; RMCA, right main coronary artery; TTE, transthoracic echocardiography; \*, p-value statistically significant.

an LCA Zmax of 3.7 SD which did not decrease on serial echocardiograms. This was considered a pseudo-dilatation caused by an anatomic variant of the LCA with a short main stem in a left dominant CA system. This confirms the observation that anatomic variations are frequent in the LCA, so the Z-score must be interpreted with caution.<sup>5</sup>

CA lesions in patients with KD are associated with pathological changes in the CA wall. Based on an analysis of autopsy cases, in the early stages of KD, edematous changes in the media and CA dilatation are elucidated.<sup>16</sup> Muniz et al described that enlargement of the proximal coronary arteries above 2.0 SD also appeared in patients suffering from febrile diseases other than KD; nevertheless, the largest dimensions have been reported in

patients with KD.<sup>17</sup> In accordance, Bratincsak et al identified no febrile control patient with Z-scores above 2.5 SD in comparing CA dimensions of KD patients and febrile control patients, suggesting that high fever caused by a common infectious disease does not lead to CA aneurysms.<sup>11</sup> The same effect could be observed in two case reports describing a transient dilation of the left main CA related to Epstein-Barr virus and Rickettsia infection, respectively.<sup>18,19</sup> Binstadt et al documented CA dilation in a case series of patients with systemic-onset juvenile idiopathic arthritis (JIA), including two patients with significant dilation (Z-score > 2.5) of the RCA. Several of their patients were initially suspected of having KD, but none of their patients developed CA aneurysms, and all of the CA dimensions normalized.<sup>12</sup> This suggests that in case of prolonged and severe systemic inflammation such as JIA, the arterial wall can also be involved in the inflammatory process and CA dilation can occur at least transiently. The pathogenesis of increased CA dimensions in FC has not yet been fully clarified; it may be related to higher myocardial oxygen demand caused by fever and tachycardia. The subsequent increase in coronary blood flow results mainly from compensatory dilation of the coronary arterioles (the coronary resistance vessels) but not the proximal segment of major branches.<sup>20</sup>

A CA Z-score at or above the threshold of 2.5 SD is considered a strong indication of KD.<sup>5</sup> However, our efforts should be aimed at preventing such a pronounced dilatation of a CA in the first place. To confirm diagnosis of KD, it is not necessary to detect dilation or aneurysms. We were able to diagnose CA involvement in KD patients early by demonstrating a significant increase of CA internal diameters by serial echocardiograms. In contrast, there was even a slight decrease in CA dimensions in serial measurements in the FC group. Our observation suggests that patients suspected having KD should be monitored with serial echocardiograms to detect a progressive enlargement of the CA diameters, even if initial Z-scores are within the normal range. It is mandatory that in cases with clinical or laboratory findings strongly suggesting KD, therapy should be initiated even with normal echocardiographic results.

There are several limitations of the present study that should be addressed. First, this is a retrospective study and was performed at a single institution. Second, the study included a relatively small number of patients due to the low prevalence of KD in Germany.<sup>21</sup> Third, we did not test interobserver variability.

## Conclusion

BSA-adjusted CA dimensions (Z-scores) in FC were below 2.5 SD in 96% and thus significantly smaller than those in KD patients. The results of serial echocardiograms in the acute phase revealed a mild decrease of CA internal diameters in FC patients, whereas serial pretreatment CA dimensions in KD patients showed a significant increase. Our study indicates that CA dimensions in children with common febrile illnesses very rarely exceed a Z-score threshold of 2.5 SD according to the equation of Dallaire and Dahdah.<sup>15</sup> Consequently, a CA Z-score  $\geq 2.5$  SD in single or serial echocardiography can support the diagnosis of KD in children with an acute febrile illness who do not meet the clinical criteria for the diagnosis of complete KD. We therefore recommend a clinical approach with serial measurements of CA Z-scores in the acute phase of febrile children with suspected KD.

## Abbreviations

SD	standard deviation
BSA	body surface area
CA	coronary artery
KD	Kawasaki disease
FC	febrile children with other illnesses than KD
LCA	left main coronary artery
LAD	left anterior descending artery
LCX	left circumflex coronary artery
RCA	right main coronary artery
TTE	transthoracic echocardiography

### Note

The study was approved by the Institutional Review Board of the University of Regensburg (file number 14-101-0206).

### Authors' Contribution

S.G. was responsible for examination and data collecting, wrote, and edited the manuscript. M.H. collected data, wrote, and edited the manuscript; T.G. wrote, reviewed, and edited the manuscript. R.Z. wrote, reviewed, and edited the manuscript. M.J.D. contributed to examination and data collection. M.M. and H.M. conceptualized the study design and reviewed and edited the manuscript. All authors contributed to manuscript revision, read, and approved the final version.

### Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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