Arch Rheumatol 2024;39(4):549-557
doi: 10.46497/ArchRheumatol.2024.10546

ORIGINAL ARTICLE

Long-term health-related quality of life in Kawasaki disease complicated with coronary artery aneurysm in the Nanjing region of China: Results of the largest single-center assessment

Wenting Gao, Ying Meng, Yu Chen, Mei Chen

Department of Cardiovascular Medicine, Children's Hospital of Nanjing Medical University, Nanjing, China

Correspondence: Mei Chen, MD.
E-mail: chenmlilac@163.com

Received: October 26, 2023
Accepted: May 17, 2024
Published online: December 12, 2024

Citation: Gao W, Meng Y, Chen Y, Chen M. Long-term health-related quality of life in Kawasaki disease complicated with coronary artery aneurysm in the Nanjing region of China: Results of the largest single-center assessment. Arch Rheumatol 2024;39(4):549-557. doi: 10.46497/ArchRheumatol.2024.10546.

ABSTRACT

Objectives: The study aimed to compare the long-term health-related quality of life in children with Kawasaki disease (KD) with and without coronary artery aneurysms (CAAs) in the largest pediatric medical center in the Nanjing region of China.

Patients and methods: The retrospective study included a total of 107 patients (54 males, 53 females; mean age: 3.4±1.8 years; range, 2.12 to 1.75 years) between January 2012 and December 2022. Among these patients were a cohort of 64 child patients diagnosed with CAAs due to KD and a control group of 43 hospitalized child patients with KD without CAAs. The children with CAAs were divided into two groups according to the size of their aneurysms: the aneurysm group and the giant aneurysm group. Both child-reported and parent/proxy-reported Pediatric Quality of Life Inventory surveys were collected at baseline and during long-term follow-up.

Results: The median follow-up duration was 5.58 years (range, 1.03 to 10.67 years). The mean age at the time of diagnosis was 3.43±1.75 years (range, 2.12 to 12.19 years). At baseline, children reported a total score of 48.63±16.60 and parents reported a mean score of 46.76±14.77 in the giant aneurysm group. The child-reported and parent/proxy-reported outcomes were 54.71±15.82 and 52.73±13.34 in the aneurysm group and 48.30±28.24 and 46.35±15.79 in the control group, respectively. In long-term follow-up, children in the aneurysm group reported a mean score of 81.61±19.50, which was 9.70 (95% confidence interval (CI): 2.22-17.18) points higher than that of the control group (p=0.014) and 9.51 (95% CI: 2.02-16.98) points lower than that of the giant aneurysm group (p=0.012). Similarly, parents reported a mean score of 81.03±12.57 in the aneurysm group, which was significantly lower than that of the control group (p=0.010) and significantly higher than that of the giant aneurysm group (p=0.009).

Conclusion: A proportion of children presenting with CAAs without complete recovery often encountered issues that disrupted their well-being during long-term follow-up. Therefore, routine outpatient health-related quality of life screening might be set as an appropriate supportive service to assist in identifying patients with a history of CAAs to eliminate the risk for long-term disabilities following the initial clinical improvement.

Keywords: Coronary artery aneurysms, health-related quality of life, Kawasaki disease, pediatric quality of life inventory.

Kawasaki disease (KD) is an acute self-limited vasculitis with an intense inflammatory process accounting for the most common cause of acquired heart disease in children mostly below five years of age.[1] The epidemiological surveys from China reported an increasing trend in the incidence of KD, and data from Beijing and Shanghai were documented to be about 46.3 to 55.1 per 100,000 in cases aged <5 years during the past decades.[2] The diagnosis of KD is challenging given the variety of clinical symptoms based on the presence of fever and a cluster of mucocutaneous manifestations, which usually creates difficulties and delays clinical treatment.[3] During the acute phase, there is a predilection for cardiovascular complications such as valvulitis, myocarditis, pericarditis, and KD syndrome. About 15 to 25% of children develop coronary artery aneurysms (CAAs) in the subacute to convalescent phase, leading to significant long-term consequences, including aneurysm, arterial thrombotic occlusion, or even sudden death if left untreated.[4,5] Nevertheless, prompt treatment with high-dose intravenous

immunoglobulin (IVIG) infusion within the first 10 days of illness reduces the incidence of aneurysm to between 3 and 5%.[6] Besides cardiac complications, neurological symptoms such as extreme irritability, seizures, hemiplegia, facial palsy, and aseptic meningitis were also occasionally reported. Therefore, children with KD experience a considerable amount of illness burden leading to impairment of their function in a variety of aspects of life. Although the majority recover after the acute phase of KD, the children who develop CAAs may have to face long-term daily impairment on health-related quality of life (HR-QoL) due to potentially severe cardiovascular sequelae. However, the impact of acute and chronic KD on HR-QoL encompassing the physical, psychological, and social domains in children is not well-documented in the literature.

We hypothesized that children with KD exhibit different quality of life due to the vague long-term prognosis of coronary artery lesions (CALs). Therefore, the study was conducted in the largest center of the Nanjing region in China to investigate the HR-QoL during the acute phase and a 10-year, long-term follow-up.

PATIENTS AND METHODS

The retrospective cohort study assessed 745 patients diagnosed with KD at the Department of Cardiovascular Medicine and Respiratory Medicine, Children's Hospital of Nanjing Medical University between January 2012 and December 2022. A written informed consent was obtained from the parents and/or legal guardians of the patients. The study protocol was approved by the IEC of Children's Hospital of Nanjing Medical University Ethics Committee (date: 16.09.2023, no: 202309016-1). The study was conducted in accordance with the principles of the Declaration of Helsinki. Patients diagnosed with KD according to the diagnostic criteria[7] at our institution were considered eligible if they met the following criteria: *(i)* being aged 0 to 18 years; *(ii)* the presence of CAA during acute KD diagnosed by echocardiography; *(iii)* having complete medical data of hospitalization during the acute phase of KD. Patients who had incomplete KD, severe chronic illness, immunological dysfunction unrelated to KD, or mental disorders were excluded. Seventy-one patients met the inclusion criteria, and a control group (n=49) of age-and sex-matched KD patients without CAAs was created. The KD patients with CAA were divided into two groups based on the Z-score definition: the aneurysm group (patients with a small-sized CAA with a Z-score of 2.5 to 5 or a medium-sized CAA with a Z-score of 5 to 10) and the giant aneurysm group (patients whose coronary artery dilation met a Z-score ≥10 with or without ischemic symptoms).[8] The Cardio Z software (Circle Cardiovascular Imaging Inc., Calgary, Canada), as described by Dallaire and Dahdah,[9] was employed to calculate the Z-score, and CAAs were predefined as a maximum Z-score ≥2.5 of the proximal right coronary artery or proximal left anterior descending artery on echocardiogram.[10] Two patients in the aneurysm group and six patients in the control group were excluded due to missing questionnaires. Thus, the study was conducted with a total of 107 participants (54 males, 53 females; mean age: 3.4±1.8 years; range, 2.12 to 1.75 years). A detailed flowchart of the patient selection process is presented in Figure 1.

Demographic, clinical, and echocardiographic data of all participants, including age, sex, date of KD onset, duration of hospital admission, interval from KD onset to the study, and CAA outcome during acute phase, and persistent CAA at follow-up, were retrospectively retrieved from a review of electronic medical record system. The multidimensional HR-QoL was assessed using the previously validated instrument of Pediatric Quality of Life Inventory (PedsQL), which integrates generic core scales and disease-specific modules into one measurement system for children aged 0 to 18 in general health status or with acute and chronic health conditions. The fourth version of PedsQL comprises 23 items in four categories: *(i)* physical functioning (8 items), *(ii)* emotional functioning (5 items), *(iii)* social functioning (5 items), and *(iv)* school functioning (5 items). Each answer is scored on a 5-point scale: 0=never a problem, 1=almost never a problem, 2=sometimes a problem, 3=often a problem, and 4=almost always a problem. The reverse scores for 23 items are summarized ranging from 0 to 100 with higher scores indicating higher HR-QoL. Both the self-reported format for ages 5 to 18

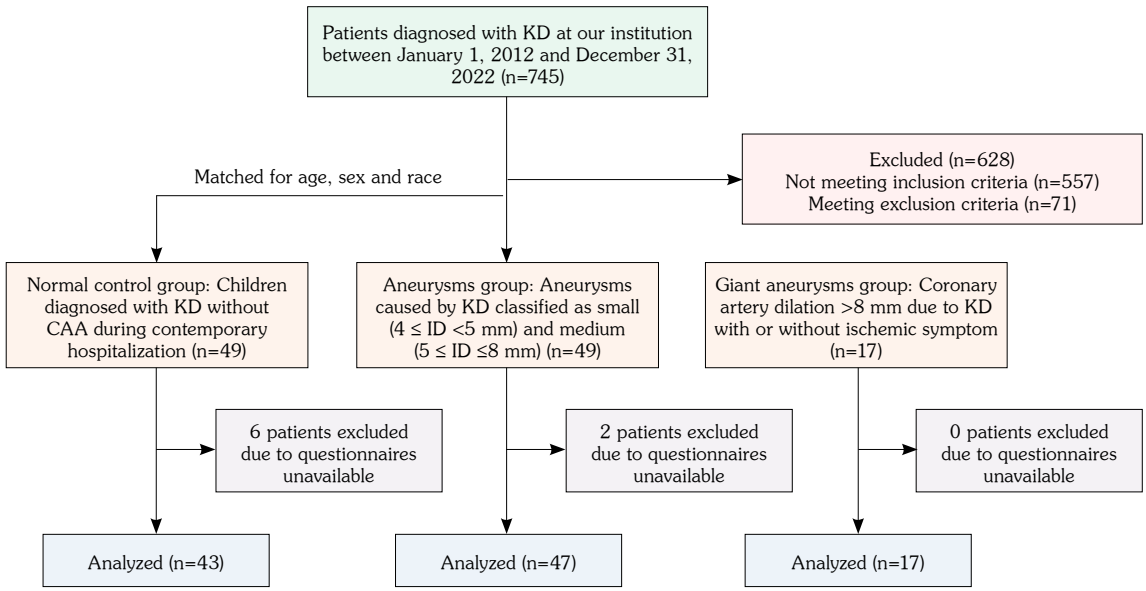

Figure 1. Patient selection flowchart.
KD: Kawasaki disease; ID: Internal diameter; CAA: Coronary artery aneurysm.

and the parent/proxy-reported format for ages 0 to 4 were used in the present study.[11]

According to our routine treatment, the baseline scores reflecting HR-QoL within one month of disease onset were collected within 72 h of hospital admission. For the long-term HR-QoL measurements, four investigators blinded to the KD cases or control subjects were available to answer the PedsQL for each participant (ages 5 to 18) or the parents of each participating child (ages 2 to 5) to complete the self-administered instruments by telephone. A total of three attempts would be made to verify the long-term follow-up assessment for all enrolled cases.

Statistical analysis

Sample size was calculated using PASS software version 16.0 (NCSS LLC., Kaysville, UT, USA). According to consensus after a series of expert discussion based on our clinical experience, a set of Tukey-Kramer pair-wise multiple comparison test were conducted for detecting a 30-point difference in mean scores (55 in the giant aneurysm group *vs.* 85 to 95 in the other two groups), with the largest standard deviation (SD) of 35. A sample size of 115 (17 in the giant aneurysm group and 49 in each of the other three groups, with a group sample size ratio of 3:3:1) was calculated to provide a power of 90% with type 1 error of 5% and a dropout rate of 20% using a simulation of 1,000 interactions.

Statistical analyses were performed with the IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov Z test was employed for the normality check. Categorical data, normally distributed, data and nonnormally distributed data were expressed as percentages, mean ± standard deviation (SD), and median (interquartile range) and compared using the chi-square test, Mann-Whitney U test, and analysis of covariance models adjusted for the baseline score and matching variables, respectively. A p-value <0.05 was considered statistically significant.

RESULTS

Table 1 illustrates the characteristics of the enrolled participants. The mean age at the time of diagnosis for KD was 3.43±1.75 years (range, 2.12 to 12.19 years). A total of 107 PedsQL questionnaires were available, consisting of 68 child-reported and 41 parent/proxy-reported data at the time of

Table 1. Baseline characteristics of KD patients with giant aneurysms or aneurysms and KD patients without CAA as the control group

	Giant aneurysms - Control matched cohorts					Giant aneurysms - Aneurysms cohorts				
	Giant aneurysms (n=17)		Control (n=43)			Giant aneurysms (n=17)		Aneurysms (n=47)		
Variables	n	%	n	%	*p*	n	%	n	%	*p*
Age (year)					0.807					0.665
<1	5	29.4	14	32.6		5	29.4	18	38.3	
≥1, <5	8	47.1	22	51.2		8	47.1	22	46.8	
≥5	4	23.5	7	16.3		4	23.5	7	14.9	
Sex Female	4	23.5	25	58.1	0.022	4	23.5	20	42.6	0.244
Race					0.809					0.525
Han Chinese	14	82.4	35	81.4		14	82.4	34	72.3	
Minority	3	17.6	8	18.6		3	17.6	13	27.7	
Residential address					0.779					0.774
Cities and towns	10	58.8	23	53.5		10	58.8	30	63.8	
Rural	7	41.2	20	46.5		7	41.2	17	36.2	
Body mass index (kg/m^2)					0.916					0.851
>23.9	4	23.5	10	23.3		4	23.5	9	19.1	
18.5-23.9	7	41.2	20	46.5		7	41.2	23	48.9	
<18.5	6	35.3	13	30.2		6	35.3	15	31.9	
Duration of fever (days) (median [IQR])	10 (8-13)		5 (3-7)		<0.001	10 (8-13)		8 (5-11)		0.132
Resistant to IVIG treatment	4	23.5	1	2.3	0.020	4	23.5	6	12.8	0.435
Time to initial echocardiogram (days) (median [IQR])	6 (5-7)		7 (6-8)		0.132	6 (5-7)		6 (5-7)		0.256
Admission to the pediatric intensive care unit	5	29.4	2	4.8	0.017	5	29.4	7	114.9	0.276
Duration of hospital admission (days) (mean±SD)	16.43±5.97		7.01±3.73		<0.001	16.43±5.97		8.91±1.52		<0.001

KD: Kawasaki disease; CAA: Coronary artery aneurysms; IQR: Interquartile range; SD: Standard deviation; IVIG: Intravenous immunoglobulin.

Table 2. Comparison of PedsQL scores at baseline and long-term follow-up in KD patients with giant aneurysms and small/medium aneurysms and the matched KD patients without aneurysms

				p			*p*			*p*			*p*			*p*	
Time	Formats	Group	Total scores	5%	1%	Physical health	5%	1%	Emotional functioning	5%	1%	Social functioning	5%	1%	School functioning	5%	1%
Baseline	Child self-report	GA (n=2)	48.63±16.60	a	A	48.23±16.51	a	A	45.61±14.32	a	A	42.62±11.98	a	A	44.63±13.37	a	A
		A (n=9)	54.71±15.82	a	A	53.75±13.89	a	A	50.73±12.14	a	A	50.75±12.24	a	A	49.25±10.43	a	A
		C (n=5)	48.30±28.24	ab	AB	47.19±16.99	ab	AB	43.53±13.89	ab	AB	44.37±14.06	ab	AB	46.36±16.82	ab	AB
	Parent-proxy report	GA (n=15)	46.76±14.77	a	A	45.32±13.34	a	A	44.35±12.18	a	A	41.23±10.14	a	A	43.50±11.59	a	A
		A (n=38)	52.73±13.34	a	A	52.25±12.03	a	A	48.73±9.63	a	A	42.85±13.33	a	A	43.64±13.84	a	A
		C (n=38)	46.35±15.79	ab	AB	45.81±15.41	ab	AB	44.56±12.63	ab	AB	48.16±12.79	ab	AB	47.68±19.66	ab	AB
Long-term follow-up	Child self-report	GA (n=14)	71.36±17.41	a	A	68.31±19.27	a	A	70.96±19.02	a	A	77.57±17.62	a	A	77.52±17.60	a	A
		A (n=36)	81.61±19.50	b	A	83.64±11.18	b	B	80.52±10.09	b	A	85.28±10.64	b	A	85.31±11.58	b	A
		C (n=29)	90.90±17.14	c	BC	92.75±14.03	c	BC	88.93±16.19	c	BC	92.43±13.29	c	BC	90.48±12.17	c	BC
	Parent-proxy report	GA (n=3)	65.93±13.69	a	A	66.42±19.63	a	A	72.94±16.97	a	A	75.73±17.27	a	A	68.36±10.82	a	A
		A (n=11)	81.03±12.57	b	A	84.57±11.09	b	A	85.69±11.69	b	A	86.23±11.65	b	A	84.13±10.94	b	B
		C (n=14)	92.85±10.72	c	BC	92.60±14.38	c	BC	92.10±15.19	cd	BC	93.89±12.72	c	BC	90.27±14.69	c	BC

PedsQL: Pediatric Quality of Life Inventory; KD: Kawasaki disease; GA: Giant aneurysms; A: Small-sized or medium-sized aneurysms; C: Coronary artery aneurysms; b: The lower letters and upper letters represent the statistical significance at 5% and 1%, respectively; the same lower letters between treatments indicates no significant difference ($p>0.05$); absence of the same upper letter indicates a highly significant difference ($p\leq0.01$); presence of the same upper letter without the same lower letters indicates a significant difference with $0.05 \geq$ p value >0.01.

long-term follow-up, with a median follow-up of 5.58 years (range, 1.03 to 10.67 years). At baseline, children reported a total score of 48.63±16.60 and parents reported a mean score of 46.76±14.77 in the giant aneurysms group. In the control group, children reported a mean score of 48.30±28.24, and the parent/proxy-reported mean score was 46.35±15.79, which were comparable to those in the giant aneurysm group (p=0.427 and p=0.161, respectively). Among the aneurysm group, the mean total scores were also comparable to the giant aneurysm group (54.71±15.82 for the child-reported questionnaire, p=0.969; 52.73±13.34 for the parent/proxy-reported questionnaire, p=0.741). No significant differences were found between the giant aneurysm group and the control group or the aneurysm group and the control group in the detailed scores from the subscales of functioning assessments in PedsQL at baseline (Table 2).

Starting at baseline, the total HR-QoL scores improved over time in the total sample. In addition, within each subgroup, scores also significantly improved over time. In the long-term follow-up, the children in the aneurysm group reported a mean total score of 81.61±9.50, which was lower than that of the control group (9.51; 95% confidence interval [CI]: 2.02-16.98; p=0.014) and 9.70 (95% CI: 2.22-17.18) points higher than that of the giant aneurysm group (p=0.012). Similar to the children, parents reported a mean score of 81.03±2.57 in the aneurysm group, which was significantly higher than that of the giant aneurysm group (71.03±3.63, p=0.009) and statistically significantly lower (–9.9 points; 95% CI: -17.27 - –2.53) than that of the control group (p=0.010). Analysis of the four functioning subscales revealed that patients in the giant aneurysm group reported the lowest scores for both the child-reported and parent/proxy-reported formats, while the matched control group showed the highest scores (Table 2).

DISCUSSION

Although the incidence of KD in the Nanjing region of China remains uncertain due to the lack of accurate population statistics and a centralized database, our hospital, as the largest referral center for the treatment of coronary artery sequelae due to KD, has admitted the vast majority of sick children in the Nanjing region. However, studies investigating the long-term HR-QoL consequences of cardiovascular sequelae of KD in children are scarce. Our results established comprehensive comparisons of long-term HR-QoL between KD children with CAAs and control subjects without CAAs during hospitalization, and we found that coronary artery sequelae had a negative influence on a patient's life. The HR-QoL during the long-term follow-up of children with a history of CAAs, particularly giant ones in the acute KD phase, was significantly impaired.

Since it was first described in Japan in 1967 by Kawasaki,[12] the KD disease has surpassed acute rheumatic fever as the leading cause of acquired heart disease among young children. The etiology remains poorly understood; it appears to be an interplay of genetic susceptibility and infectious triggers followed by an abnormal immune response, which mainly results in multisystemic vasculitis, showing a predilection for the coronary arteries.[13] Usually, children suffering from KD experience a considerable amount of functional impairment from the disease's sudden onset due to a constellation of clinical signs, including fever, diffuse mucosal inflammation, conjunctivitis, lymphadenopathy, angioedema, and skin rashes. However, the diagnosis of KD can often be challenging due to both its broad spectrum of clinical features and atypical presentations.[14] Therefore, possible delays in diagnosis and treatment occurred in many children due to the lack of typical manifestations, which challenges both the young patient and their parents with physical and psychological consequences of having suffered from a significant disease of unknown etiology and future outcome.[3] Additionally, it was described that extreme irritability was a common symptom during the acute phase of KD, and children were usually characterized by an overwhelming range of emotions, which also led to a heavy negative influence on a patient's life.[15] Previous data compared KD caregivers' perceptions of their child's health with other common childhood diseases and found that HR-QoL plummets dramatically after hospital

admission due to the acute KD episode.[16] Consistent with the mentioned published trials, our data emphasized that children with highly variable clinical presentation of acute KD on admission suffered greater physical, social, emotional, and school functioning disabilities.

During the acute phase of KD, the aim of treatment is to reduce inflammation in the coronary artery and prevent coronary thrombosis. The risk of coronary artery involvement was reported in nearly 25% of cases if left untreated. Although IVIG administration was established as a standard therapy for KD, approximately 10 to 20% of patients showed resistance or had recurrent fever within 36 to 48 h after IVIG.[7] Despite early treatment with IVIG, which was considered the most important determining factor for the development of CAA, a few children would still suffer from the CAAs, ranging from transient mild dilation to persistent aneurysms or giant CAA, occurring in up to 5 to 7%.[17,18] As a result, the prevalence of CAAs, particularly giant ones, exposed patients to the risk of coronary arterial stenosis, obstruction, and thrombosis leading to consequent angina pectoris or even myocardial infarction and sudden death.[19] Acute necrotizing arteritis in the acute phase of KD quickly destroys the normal structure of the coronary arteries in a few days compared to five decades of lifetime atherosclerosis and results in the dilation of the weakened coronary arteries.[20] On the other hand, chronic inflammation and luminal myofibroblastic proliferation involving smooth muscle cell-derived myofibroblasts during the long term have the potential to reduce the size and normalize the coronary artery lumen morphology.[7] Although most patients have not been followed long enough to evaluate the long-term natural course of CAAs after acute KD, many CAAs were reported to regress to a normal-sized diameter, and the likelihood of regression appears to be highly dependent on the original CAA size.[21] A large Japanese study showed that 55 to 60% of patients had CAA regression typically within one to two years after the acute phase by analyzing serial angiograms in KD patients with CAA.[22] However, none of the patients with giant aneurysms had a regression in their study. Similarly, a two-center retrospective study with a large sample also found that CAA size at diagnosis was highly associated with the prediction of CAA regression, with a low regression rate of 16% in patients with large/giant CAA, and a high regression rate of 85% in those with small or medium CAA.[23] However, a previous study emphasized that the long-term consequences of these changes are still largely unknown; although many patients with CAA regressed from aneurysmal dilatation, the coronaries remain abnormally thickened, and vessel-wall calcification is often detected.[24] Chahal et al.[25] reviewed the caregivers of children with CAAs and found that the principal reason for persistent anxiety derived from the uncertainty of prognosis implied by the degree of CAAs. Accordingly, research on the long-term HR-QoL has demonstrated discrepant results among cases only with a remote history of KD and patients with CAAs.[17] Our findings were consistent with these results, which reported that there was a significant improvement of HR-QoL over time in all cohorts, whereas a statistically significant difference was found in all domains of the PedsQL score among the three cohorts at the long-term follow-up. The long-term HR-QoL scores in patients with small or medium coronary aneurysms were significantly lower than those diagnosed with KD without CAAs and significantly higher than those in the giant aneurysm group. All the mentioned results support the previous perspective that the majority of the patients recover fully and do not face long-term cardiac consequences of KD after the acute phase. However, the presence of giant aneurysms was associated with the worst long-term HR-QoL. Previous data showed that the presence of CAAs would add potentially severe cardiovascular sequelae with vague long-term prognosis. According to our results, the burden of CAAs after acute KD could become a significant contributory factor to possible long-term disabilities. Therefore, it could prolong uncertainty and cause physical and psychological distress to patients' long-term life quality. These findings are consistent with previous research aimed to identify significant changes in physical and psychological health as perceived by the caregiver of children with a history of KD. Their results also demonstrated a similar trend in which patients and their caregivers suffer considerable anxiety during the long-term follow-up despite the mostly favorable prognosis. Therefore, we believe that our data support our principal hypothesis by revealing that the long-term HR-QoL findings

reflected that a proportion of children presenting with CAAs without complete recovery during long-term follow-up often encountered issues disrupting their well-being. Considering the long-term follow-up outcomes, despite the surveillance of outpatients for monitoring the development of acquired heart disease, routine outpatient HR-QoL screening might be employed as an appropriate supportive service to assist in identifying patients with CAAs to eliminate the risk for long-term disabilities following initial clinical improvement.

There are some limitations to this study. First, due to the nature of the retrospective analysis, there might be some undetected confounders and probable bias. Second, the study was conducted within a single center; therefore, the results may not be generally applicable. Third, the patients' limited awareness of their disease, given their young age during the acute phase, poses challenges in accurately responding to the questionnaires. Finally, only total PedsQL scores were reported as a primary outcome measure instead of individual subscales for physical, psychosocial, emotional, social, and school functioning. Future large-scale, long-term randomized studies are needed to validate our findings.

In conclusion, despite HR-QoL scores improving with time, a proportion of children presenting with CAAs during acute KD often encountered issues that disrupted their well-being during long-term follow-up due to incomplete recovery. Therefore, the routine outpatient HR-QoL screening might be set as an appropriate supportive service to assist in identifying those with a history of CAAs to eliminate the risk for long-term disabilities following the initial clinical improvement.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Conceptualization, methodology, validation, formal analysis, investigation, data curation, writing - original draft, supervision: M.C.; Methodology, validation, formal analysis, investigation, data curation, writing - original draft: W.G.; Methodology, validation, formal analysis, investigation, data curation, writing - original draft: Y.M.; Data curation, writing-original draft preparation: Y.C.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Wood LE, Tulloh RM. Kawasaki disease in children. Heart 2009;95:787-92. doi: 10.1136/hrt.2008.143669.
2. Jiao F, Jindal AK, Pandiarajan V, Khubchandani R, Kamath N, Sabui T, et al. The emergence of Kawasaki disease in India and China. Glob Cardiol Sci Pract 2017;2017:e201721. doi: 10.21542/gcsp.2017.21.
3. Zhu F, Ang JY. 2021 update on the clinical management and diagnosis of Kawasaki disease. Curr Infect Dis Rep 2021;23:3. doi: 10.1007/s11908-021-00746-1.
4. Barut K, Sahin S, Kasapcopur O. Pediatric vasculitis. Curr Opin Rheumatol 2016;28:29-38. doi: 10.1097/BOR.0000000000000236.
5. Lee JJY, Lin E, Widdifield J, Mahood Q, McCrindle BW, Yeung RSM, et al. The long-term cardiac and noncardiac prognosis of Kawasaki disease: A systematic review. Pediatrics 2022;149:e2021052567. doi: 10.1542/peds.2021-052567.
6. Newburger JW, Takahashi M, Burns JC, Beiser AS, Chung KJ, Duffy CE, et al. The treatment of Kawasaki syndrome with intravenous gamma globulin. N Engl J Med 1986;315:341-7. doi: 10.1056/NEJM198608073150601.
7. McCrindle BW, Rowley AH, Newburger JW, Burns JC, Bolger AF, Gewitz M, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association. Circulation 2017;135:e927-99. doi: 10.1161/CIR.0000000000000484.
8. Manlhiot C, Millar K, Golding F, McCrindle BW. Improved classification of coronary artery abnormalities based only on coronary artery z-scores after Kawasaki disease. Pediatr Cardiol 2010;31:242-9. doi: 10.1007/s00246-009-9599-7.
9. Dallaire F, Dahdah N. New equations and a critical appraisal of coronary artery Z scores in healthy children. J Am Soc Echocardiogr 2011;24:60-74. doi: 10.1016/j.echo.2010.10.004.
10. McCrindle BW, Li JS, Minich LL, Colan SD, Atz AM, Takahashi M, et al. Coronary artery involvement in children with Kawasaki disease: Risk factors from analysis of serial normalized measurements. Circulation 2007;116:174-9. doi: 10.1161/CIRCULATIONAHA.107.690875.
11. Gheissari A, Farajzadegan Z, Heidary M, Salehi F, Masaeli A, Mazrooei A, et al. Validation of Persian version of PedsQL™ 4.0™ generic core scales in toddlers and children. Int J Prev Med 2012;3:341-50.

12. Kawasaki T. Acute febrile mucocutaneous syndrome with lymphoid involvement with specific desquamation of the fingers and toes in children. Arerugi 1967;16:178-222. Japanese.
13. Agarwal S, Agrawal DK. Kawasaki disease: Etiopathogenesis and novel treatment strategies. Expert Rev Clin Immunol 2017;13:247-58. doi: 10.1080/1744666X.2017.1232165.
14. Zhu FH, Ang JY. The clinical diagnosis and management of Kawasaki disease: A review and update. Curr Infect Dis Rep 2016;18:32. doi: 10.1007/s11908-016-0538-5.
15. Liu X, Zhou K, Hua Y, Wu M, Liu L, Shao S, et al. Neurological involvement in Kawasaki disease: A retrospective study. Pediatr Rheumatol Online J 2020;18:61. doi: 10.1186/s12969-020-00452-7.
16. van Oers HA, Tacke CE, Haverman L, Kuipers IM, Maurice-Stam H, Kuijpers TW, et al. Health related quality of life and perceptions of child vulnerability among parents of children with a history of Kawasaki disease. Acta Paediatr 2014;103:671-7. doi: 10.1111/apa.12619.
17. Galeotti C, Bayry J, Kone-Paut I, Kaveri SV. Kawasaki disease: Aetiopathogenesis and therapeutic utility of intravenous immunoglobulin. Autoimmun Rev 2010;9:441-8. doi: 10.1016/j.autrev.2009.12.004.
18. Varol F, Dedeoğlu R, Kiliç A, Bakar MT, Adrovic A, Şahin S, et al. Retrospective analysis of children diagnosed with Kawasaki disease. Turk J Med Sci 2023;53:979-89. doi: 10.55730/1300-0144.5662.
19. Newburger JW, Takahashi M, Gerber MA, Gewitz MH, Tani LY, Burns JC, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: A statement for health professionals from the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. Circulation 2004;110:2747-71. doi: 10.1161/01.CIR.0000145143.19711.78.
20. Dahdah N. A tale of a trail on how it takes 5 days of Kawasaki disease to initiate coronary artery injury and change the lives of children. Turk Arch Pediatr 2024;59:131-4. doi: 10.5152/TurkArchPediatr.2024.23254.
21. Tsuda E, Hashimoto S. Time course of coronary artery aneurysms in Kawasaki disease. J Pediatr 2021;230:133-9.e2. doi: 10.1016/j.jpeds.2020.12.004.
22. Kato H, Sugimura T, Akagi T, Sato N, Hashino K, Maeno Y, et al. Long-term consequences of Kawasaki disease. A 10- to 21-year follow-up study of 594 patients. Circulation 1996;94:1379-85. doi: 10.1161/01.cir.94.6.1379.
23. Friedman KG, Gauvreau K, Hamaoka-Okamoto A, Tang A, Berry E, Tremoulet AH, et al. Coronary artery aneurysms in Kawasaki disease: Risk factors for progressive disease and adverse cardiac events in the US population. J Am Heart Assoc 2016;5:e003289. doi: 10.1161/JAHA.116.003289.
24. Daniels LB, Gordon JB, Burns JC. Kawasaki disease: Late cardiovascular sequelae. Curr Opin Cardiol 2012;27:572-7. doi: 10.1097/HCO.0b013e3283588f06.
25. Chahal N, Jelen A, Rush J, Manlhiot C, Boydell KM, Sananes R, et al. Kawasaki disease with coronary artery aneurysms: Psychosocial impact on parents and children. J Pediatr Health Care 2017;31:459-69. doi: 10.1016/j.pedhc.2016.11.007.