ARTICLE

Long-term Consequences of Kawasaki Disease Among First-Year Junior High School Students

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Objective: To determine whether height, weight, and electrocardiographic (ECG) abnormalities differ at the age of 13 years between adolescents with and without Kawasaki disease (KD) (also known as mucocutaneous lymph node syndrome).

Design: A population-based cohort study.

Setting: School community and public health service.

Methods: Data from the nationwide surveys of KD in Japan were linked with those of junior high school cardiac screening in Tochigi Prefecture between April 1, 1986, and June 30, 1998 (except data for 1988 and 1994). Using this database, students with KD and students without KD in the first year of junior high school were compared.

Main Outcome Measures: Height, weight, and ECG abnormalities.

Results: Eight hundred sixty students (486 adolescent boys and 374 adolescent girls) with KD and 308 729 students (158 193 adolescent boys and 150 536 adolescent girls) without KD were located. There was no difference in average height and weight between the students with and without KD (using the *P* values for a *t* test of the means). The proportion of abnormal ECG findings was 10% and 3% among those with and without KD, respectively.

Conclusion: Even at age 13 years, the proportion of abnormal ECG findings was about 3 times higher among adolescents with KD (using a χ^2 test of the difference in 2 binomial proportions).

Arch Pediatr Adolesc Med. 2002;156:77-80

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KAWASAKI disease (KD) (also known as mucocutaneous lymph node syndrome) is an acute febrile illness with mucosal inflammation, rash, and cervical lymphadenopathy that is recognized most often in children younger than 4 years.[1,2] The disease affects mainly small and medium arteries, particularly the coronary artery. The long-term clinical concern with KD is with the coronary artery lesions, which may result in aneurysm formation, thrombotic occlusion, and progression to ischemic heart disease.[3-5] In Japan and North America, KD is the main cause of acquired heart disease in children.[6] Some investigators[7,8] have reported on the long-term consequences and the natural history of the cardiac sequelae in patients with KD, which are mainly associated with coronary and valvular heart disease. However, few have focused their attention on other cardiac problems, such as arrhythmia, in patients with late-stage KD. In this study, linked data from nationwide surveys and first-year junior high school medical examinations between April 1, 1986, and June 30, 1998, are presented.

RESULTS

Among the nationwide surveys of KD, 1206 patients whose address was Tochigi Prefecture at the registry and who were born during the specified period were selected. Because the 1988 and 1994 cardiac screening data were not available, 1035 patients with KD were selected for this study. Of these patients, 860 (83%) could be linked to the data on the cardiac screenings for the first-year junior high school students. **Table 1** shows the number of students with KD by year.

The average height among the 860 students with KD was 151.1 cm for the adolescent boys (n=486) and 151.9 cm for the adolescent girls (n=374); for the 308 729 students without KD, the average height was 151.0 cm for the adoles-

SUBJECTS AND METHODS

A database on patients with KD, developed by the Japanese Kawasaki Disease Research Committee since 1970, was obtained. A survey questionnaire form and diagnostic guidelines for KD with color-printed photographs of typical clinical symptoms were sent to all pediatric departments of hospitals with 100 or more beds throughout Japan. Pediatricians were asked to review the medical records and to report all patients who satisfied the diagnostic criteria listed in the guidelines. About 140 000 patients were located by 15 nationwide surveys of the disease.

The Tochigi Educational Authority has conducted a cardiac disease screening program for first-year junior high school students in Tochigi Prefecture since 1986. Standard 12-lead electrocardiographic (ECG) findings of all students aged 13 years are collected under this program. The individual results of the screening from April 1, 1986, through June 30, 1998 (except data for 1988 and 1994, which were unavailable because the data were lost) were used.

The 2 databases were linked by using sex and date of birth, and the linked data were checked by individual full names. The detailed methods are as follows. The first-year junior high school students in 1998 were born in a 1-year period starting on April 2, 1985, and ending on April 1, 1986. All the patients with KD who (1) were born during this period and (2) lived in Tochigi Prefecture when they were affected by the disease were selected from the nationwide survey database. Then, this selected file was linked to the cardiac screening database by using sex and date of birth. Finally, a check was made to identify the linked individuals by name and to confirm the accuracy of the linkage. All of the first-year junior high school students in Tochigi Prefecture were divided into 2 groups: those with and those without KD.

Using this data set, the students with and without KD were compared. To evaluate the effects of the disease on physical growth, the average height and weight were compared, for adolescent boys and girls, using a *t* test for the comparison of means. The proportion of adolescents with ECG abnormalities was estimated for those with and without KD, and these proportions were compared using a χ^2 test.

Table 1. Students With KD*

Calendar Year	No. (%) of Patients With KD Selected From Nationwide Surveys	No. (%) of Linked Cases
1986	19	15 (79)
1987	37	30 (81)
1988	29†	NA
1989	70	59 (84)
1990	92	81 (88)
1991	91	77 (85)
1992	100	84 (84)
1993	185	143 (77)
1994	142†	NA
1995	96	79 (82)
1996	104	91 (88)
1997	126	101 (80)
1998	115	100 (87)
Total	**1035**	**860** (83)

*KD indicates Kawasaki disease; NA, data not available.
†These numbers were not included in the total.

Table 2. Abnormal ECG Findings for Students With and Without KD*

Calendar Year	No. (%) of Students With Abnormal ECG Findings†		Odds Ratio (95% Confidence Interval)
	Those With KD	Those Without KD	
1986	4 (27)	1046 (3)	11.1 (4.45-27.52)
1987	5 (17)	1137 (4)	5.5 (2.32-12.86)
1988	NA	NA	. . .
1989	3 (5)	855 (2)	2.1 (0.66-6.41)
1990	11 (14)	920 (3)	4.8 (2.69-8.56)
1991	4 (5)	807 (3)	1.9 (0.69-5.03)
1992	5 (6)	838 (3)	2.0 (0.82-4.86)
1993	9 (6)	662 (3)	2.3 (1.21-4.51)
1994	NA	NA	. . .
1995	15 (19)	846 (3)	7.0 (4.31-11.39)
1996	4 (4)	851 (3)	1.4 (0.50-3.70)
1997	13 (13)	1101 (4)	3.3 (1.87-5.65)
1998	13 (13)	1059 (4)	3.3 (1.90-5.75)
Total	**86** (10)	**10 122** (3)	3.3 (2.65-4.05)

*ECG indicates electrocardiographic; KD, Kawasaki disease; NA, data not available; and ellipses, data not applicable.
†The denominator for each percentage is different, and these values are not shown.

cent boys (n=158 193) and for the adolescent girls (n=150 536). The average weight for the adolescent boys and girls with KD was 45.0 kg and 44.7 kg, respectively; corresponding data for those without KD were 44.5 kg and 44.8 kg, respectively. There was no statistically significant difference between the 2 groups in either height (adolescent boys, $P=.26$; and adolescent girls, $P=.59$) or weight (adolescent boys, $P=.55$; and adolescent girls, $P=.82$). The comparison showed that the physical growth of those with KD was not affected by the illness.

The number and proportion of abnormal ECG findings for the students with and without KD are shown by calendar year in **Table 2**. Of the 860 students with KD, 10% exhibited abnormal ECG findings; of the 308 729 students without KD, 3% exhibited such findings. The odds ratio and the 95% confidence interval for the ratio are calculated. The proportion of abnormal ECG findings for the students with KD was about 3 times as high as for those without KD, and the difference was statistically significant. **Table 3** lists the abnormal ECG findings in detail for those with KD. An incomplete right bundle branch block and right axis deviation accounted for 49 (57%) of the 86 abnormal ECG findings.

COMMENT

Eight hundred sixty patients (83%) with KD of 1035 in Tochigi Prefecture who developed the disease in the corresponding period were selected (Table 1). It was

Table 3. Abnormal ECG Findings Among the Students With KD*

ECG Finding	No. of Students Affected
Incomplete right bundle branch block	25
Right axis deviation	24
Premature ventricular contraction	9
Abnormal T wave	5
Atrioventricular block (stage I° or II°)	3
Flat T wave	2
Left axis deviation	2
Premature atrial contraction	2
Right bundle branch block	2
Abnormal Q wave (borderline)	1
Atrioventricular nodal rhythm	1
Ventricular hypertrophy	
Left (borderline)	1
Right	1
Short PQ interval	1
ST depression	1
ST elevation	1
Tachycardia	1
Wolff-Parkinson-White syndrome	1
Unknown	3

*ECG indicates electrocardiographic; KD, Kawasaki disease.

assumed that the 860 patients with KD were followed up until they reached the first year of junior high school. One hundred seventy-five patients were not identified at follow-up. There were no specific patterns related to characteristics such as sex, age, or the rate of cardiac sequelae for the patients who had KD. Therefore, the main factor in a failure to link the database was probably that some patients had moved outside Tochigi Prefecture. According to this survey, only 4 patients had died.

The long-term prognosis of adolescents with KD, especially related to mortality, is nearly the same as that for healthy adolescents.[9,10] However, few investigators have focused their attention on the physical growth aspect. In this study, when those with KD reached the first year of junior high school, their average height and weight were calculated and compared with the averages of those without KD. The physical growth of both groups was comparable. This might be helpful for clarifying the natural history of patients with KD, ie, KD does not interfere with the physical development of these patients during childhood.

The results of this study might be a warning about cardiac involvement as a long-term clinical consequence of KD. Coronary artery lesions that may result in aneurysm formation, thrombogenesis, thrombotic occlusion, and eventual progression to ischemic heart disease have been reported.[3-5] Many pediatricians pay close attention to coronary artery sequelae. Some coronary aneurysms due to KD regress, but a few patients develop stenosis, especially those with large coronary aneurysms. Serial angiographic observation is important when observing patients with KD, but the standard 12-lead ECG findings are less sensitive for detecting and evaluating abnormalities.[11-13] Even when those with KD had ECG abnormalities, they were found only in the short-term and usually returned to normal within 2 months. Electrocardiographic findings are often considered unimportant.[7]

This study shows that students with KD are more likely than students without KD to exhibit ECG abnormalities in the first year of junior high school. Electrocardiographic readers were not aware of the student's medical history. Therefore, they were not likely to call borderline findings abnormal. There was a statistically significant difference between the 2 groups (Table 2). There were no outstanding differences in the details of the abnormal ECG findings of the 2 groups. Electrocardiographic findings such as an incomplete right bundle branch block and right axis deviation may be less meaningful, and the students who experienced arrhythmia need not be treated. However, the fact that the percentage of ECG abnormalities was higher among the students with KD may suggest possible cardiac disorder in the late stage of KD.[14]

We believe that adolescent patients with KD will become part of the pool of adult patients with heart disease. Pediatricians and internists should pay attention to KD in the future, when many children with KD grow up and reach old age. Additional long-term follow-up studies are recommended and will be essential if the problems associated with the prognosis in patients with KD are to be solved.

What This Study Adds

We studied 860 patients with KD who were followed up until they reached the first year of junior high school. Namely, students with KD were compared with students without KD. This study population is large. To our knowledge, results from this type of study were not reported previously.

Few investigators have focused their attention on the physical growth aspect of KD. In this study, when those with KD reached the first year of junior high school, their average height and weight were calculated and compared with the averages of those without KD. The physical growth of both groups was comparable. This might be helpful for clarifying the natural history of patients with KD, ie, KD does not interfere with the physical development of these patients during childhood.

We clarified the greater prevalence of abnormal ECG findings among the students with KD. We believe that it is new knowledge of the long-term consequences of KD.

Accepted for publication September 13, 2001.

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