CARDIAC FOLLOW UP OF PATIENTS WITH KAWASAKI DISEASE

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Kawasaki Disease: Cardiac Manifestations



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OBJECTIVES

1. To discuss the indications for doing 2-D Echo in a patient with Kawasaki Disease and how often should it be done.

2. If a patient is allergic to aspirin, to discuss other alternative drugs.

3. To discuss the duration of treatment, with or without aneurysm.

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Kawasaki disease: a review with emphasis on cardiovascular complications

Ricardo Duarte,^{II} Silvia Cisneros,² Gabriel Fernandez,³ Daniel Castellon,⁴ Cesar Cattani,⁵ Cíntia A Melo,⁶ and Asier Apocada⁷

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Abstract

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Kawasaki disease (KD) is an acute systemic vasculitis that is currently the leading cause of acquired heart disease in childhood in the United States. Cardiovascular complications are the major cause of morbidity, are responsible for virtually all deaths from KD and should be evaluated as soon as possible after the acute phase to establish the baseline status, in order to predict disease progression and determine adequate treatment. In selected patients, electrocardiography (ECG)-gated cardiac computed tomography (CT) and magnetic resonance (MR) imaging are valuable non-invasive techniques that can be used to help diagnose the cardiovascular complications associated with KD. In this article, we review the epidemiology, aetiology and pathogenesis, histopathology, clinical features, cardiovascular complications and imaging, focusing on the role of cardiac CT and MR on the initial assessment and follow-up of the cardiovascular complications of KD.

Cardiovascular manifestations of KD (in order of frequency) Duarte et al:

- Myocarditis (50-70%)
- Pericarditis with pericardial effusion (25%)
- Coronary artery aneurysms (15-25%, untreated)
- Systemic arterial aneurysms (2%)
- Valvular disease (esp. MR sec. rupture of chordae leading to papillary m dysfunction)
- Mild aortic root dilatation (acute phase)
- Myocardial infarct (1%)

Insights Imaging. 2010 Sep; 1(4): 223–231. Published online 2010 Jul 30

KAWASAKI DISEASE: CARDIAC INVOLVEMENT

Manifestations of cardiac involvement

- Acute
- Sub-acute phase
- Chronic Phase

CARDIOVASCULAR CHANGES Acute and Sub-acute Phase

PANCARDITIS

- Mitral regurgitation
- Tricuspid regurgitation
- Aortic regurgitation
- Myocardial dysfunction
- Pericardial effusion

CORONARY ARTERY ABNORMALITIES

- Perivascular inflammation
- Ectasia
- Aneurysm

CARDIOVASCULAR CHANGES Chronic Phase

CORONARY ARTERY ABNOMALITIES/ SEQUELAE

- Coronary artery insufficiency
- Regional and global dysfunction
- Ischemia related atrioventricular valve dysfunction
- Coronary artery stenosis
- Chronic fibrosis and thickening
- Thrombus formation

Kawasaki Disease in RP

PIDSP Journ, 1999;Vol.3:8-15 Copyright © 1999 Volume 3 No.1

A TEN YEAR REVIEW OF KAWASAKI DISEASE THE CHINESE GENERAL HOSPITAL EXPERIENCE

Doris Chua, M.D.* Marissa Cueto-Velasco, M.D. Eleanor Galvez, M.D.

ABSTRACT

Kawasaki disease presents with unusual features involving respiratory, gastrointestinal, urinary, cutaneous, skeletal and neurologic systems. This paper aims to describe the profile of Kawasaki disease patients in CGHMC. A total of 28 patients with Kawasaki disease from April 1988 to April In the Philippines, the first case of Kawasaki disease was reported by Mabilangan in 1982 ⁶ and another 2 cases by Songco in the same year.⁷ Two more cases were reported by Santos Ocampo in 1983⁸ and three cases from the Visayas in 1984.⁹ The first adolescent case was reported by Victorio in 1986.¹⁶ The first documented coronary aneurysm was reported in a 5 year old boy with Kawasaki disease by Arciaga in 1987.¹¹

1987 - The first documented coronary aneurysm – 5 year old boy with KD *ipbunyi.pidsp2016*

Kawasaki Disease in RP

TABLE 5. SUMMARY OF CARDIAC FINDINGS INKD*ACCORDING TO RISK FACTORS^

Risk Factors 1. Age<1 year	Without Cardiac Involvement n=15 47%	With Cardiac Involvement n=5 20%	
2. Sex (male)			
number	8/15	3/5	
ratio	1.14:1	1.5:1	
3. ESR >20mm/hr	100%	100%	
4. Platelet >450,000	47%	40%	
5. Duration of Fever	13%	40%	
>/=14 days	mean =9days	mean =10 days	
*KD = Kawasaki disease \Criteria set by Beiser & (Gersony		

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KAWASAKI DISEASE: THE ROLE OF ECHOCARDIOGRAPHY

- To establish a base line
- Increase suspicion of KD when clinical criteria for KD are "incomplete"
- Helpful in guiding appropriate therapy
- Surveillance for coronary artery changes and its complication

INCOMPLETE KAWASAKI DISEASE

- Higher risk for cardiovascular sequelae
- Greater in infants younger than 6 months old
- Diagnosis of incomplete KD is problematic because the correct diagnosis rests upon clinical judgment and supportive laboratory findings, but remains uncertain unless the child develops coronary artery abnormalities.
- However, a negative echo in the presence of strong clinical features does not preclude IVIg

Cardiac Involvement in KD

- It represents the most prominent cause of acquired coronary artery disease in childhood
- Transthoracic echocardiography is the diagnostic imaging modality of choice to screen for coronary aneurysms

Diagnosis and Management of Kawasaki Disease Am Fam Physician. 2015 Mar 15;91(6):365-71. Saguil, Fargo, Grogan

Recent Advances in Kawasaki Disease - Proceedings of the 3rd Kawasaki Disease Summit, Chandigarh, 2014.

Indian J Pediatr. 2016 Jan;83(1):47-52. Epub 2015 Aug 30.

Indian J Pediatr. 2016 Jan;83(1):47-52. doi: 10.1007/s12098-015-1858-4. Epub 2015 Aug 30.

Recent Advances in Kawasaki Disease - Proceedings of the 3rd Kawasaki Disease Summit, Chandigarh, 2014.

Singh S¹, Sharma D², Bhattad S², Phillip S³.

Author information

Abstract

Kawasaki disease (KD) is the most common cause of acquired heart disease in children in Japan, North America and Europe. It is now being increasingly recognized from the developing countries as well. If not diagnosed and treated in time, KD can result in coronary artery abnormalities in approximately 15-25 % cases. The long-term consequences of these abnormalities may manifest in adults as myocardial ischemia and congestive heart failure. Intravenous immunoglobulin (IVIg) remains the drug of choice for treatment of KD, but several new agents like infliximab, cyclosporine, glucocorticoids and statins are now being increasingly used in these patients. While echocardiography has been the preferred imaging modality hitherto, CT coronary angiography has emerged as an exciting new supplementary option and provides an entirely new dimension to this disease. The incidence of KD has shown a progressive increase in several countries and it is likely that this disease would impact public health programmes in the near future even in the developing countries.

Kawasaki Disease: Cardiac Involvement

- If not diagnosed and treated in time, KD can result in coronary artery abnormalities in approximately 15-25 % cases
- The long-term consequences of these abnormalities may manifest in adults as myocardial ischemia and congestive heart failure.

Recent Advances in Kawasaki Disease - Proceedings of the 3rd Kawasaki Disease Summit, Chandigarh, 2014. Indian J Pediatr. 2016 Jan;83(1):47-52. Epub 2015 Aug 30. Singh S1, Sharma D2, Bhattad S2, Phillip S3.

CORONARY ARTERY INVOLVEMENT

- Kawasaki disease is most common cause of acquired coronary disease in childhood (aneurysms and stenoses)
- Simple dilatation, aneurysms or giant aneurysms
 - 15/20 25 % incidence before IVIG
 - 4–8% incidence with IVIG
 - Giant aneurysms develop in .5 1 % even with IVIG
- Generally occurs in the acute phase of the disease
 - As soon as 7 days after fever onset (mean 11–12 days)
 - Peak internal luminal diameter reached in 4–6 weeks
 - Reported much later, even years

Advances in Kawasaki Disease

- Echocardiography has been the preferred imaging modality
- CT coronary angiography has emerged as an exciting new supplementary option and provides an entirely new dimension to this disease.

Recent Advances in Kawasaki Disease - Proceedings of the 3rd Kawasaki Disease Summit, Chandigarh, 2014. Indian J Pediatr. 2016 Jan;83(1):47-52. Epub 2015 Aug 30. Singh S1, Sharma D2, Bhattad S2, Phillip S3.

CASE: 6 MONTH OLD MALE



ECHO:

- DILATED LEFT MAIN
 CORONARY ARTERY
- PERICARDIAL EFFUSION

2nd HD



Characteristics of Coronary Abnormalities



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Coronary Artery Lesion in KD

J Epidemiol. 2014; 24(5): 427–434. Published online 2014 Sep 5. Prepublished online 2014 Jul 5. doi: <u>10.2188/jea.JE20140018</u> PMCID: PMC4150015

Language: English | Japanese

Epidemiologic Features and Prognostic Factors of Coronary Artery Lesions Associated With Kawasaki Disease Based on a 13-Year Cohort of Consecutive Cases Identified by Complete Enumeration Surveys in Wakayama, Japan

<u>Naomi Kitano (北野 尚美)</u>, ¹ <u>Hiroyuki Suzuki (鈴木 啓之)</u>, ² <u>Takashi Takeuchi (武内 崇)</u>, ² <u>Tomohiro Suenaga (末永 智浩)</u>, ² <u>Nobuyuki Kakimoto (垣本 信幸)</u>, ² <u>Shoichi Shibuta (渋田 昌一)</u>, ³ <u>Norishige Yoshikawa (吉川 徳茂)</u>, ² and <u>Tatsuya</u> <u>Takeshita (竹下 達也)</u>¹, for the Wakayama Kawasaki Disease Study Group (和歌山川崎病研究会プループ)

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Coronary Artery Lesion in KD

- The patient age at the onset of KD played an important role in the development of CALs
- Effect includes giant aneurysms, mid- or small-sized aneurysms
- Dilatation was U-shaped
- Both patients less than 11 months old (infant group) and those over 48 months old (advanced age group) had a significantly higher risk of developing CALs than patients 11 to 48 months old at disease onset

Epidemiologic Features and Prognostic Factors of Coronary Artery Lesions Associated With Kawasaki Disease Based on a 13-Year Cohort of Consecutive Cases Identified by Complete Enumeration Surveys in Wakayama, Japan <u>Naomi Kitano (北野 尚美)</u> _J Epidemiol. 2014; 24(5): 427–434. Published online 2014 Sep 5. Prepublished online 2014 Jul 5

KD Risk Factors for CAA

- Several scoring systems have been developed in order to identify the risk factors for CAA, particularly giant CAA
- Duration of fever has been consistently reported as a powerful risk factor
- Younger patient age, particularly less than 1 year of age, male sex and delayed diagnosis and treatment have also been associated with development of CAA
- Laboratory-detected conditions, including leukocytosis, thrombocytopaenia, lower haemoglobin or haematocrit and lower serum albumin, are also prominent risk factors

Duarte, Insights Imaging. 2010 Sep; 1(4): 223–231. Published online 2010 Jul 30

OCCURRENCE OF ARTERITIS IN KD

- » -CORONARY 96.0%
- » -RENAL 73.0%
- » PARATESTICULAR 22.6%
- » MESENTRIC 19.5%
- » PARAOVARIAN 16.6%
- » -PANCREATIC 14.6%
- » -HEPATIC 12.5%
- » -ILIAC 11%
- » -SPLENIC 10.4%
- » -AORTIC 06.2%



KAWASAKI DISEASE: Quantitative Assessment



	Internal Vessel Diameter (AHA)	Z score
Small to Medium	>3 mm - <6 mm	+3 to +7
Large	> / =6 mm	
Giant	>8 mm	> / = +10

CORONARY ARTERY DISEASE

- Aneurysms typically develop in the proximal segments
- May have thrombosis, myointimal fibrosis, and stenosis
- Myocardial ischemia, infarction, or sudden death
- Myocardium can be affected without coronary disease
- Japanese Ministry of Health Criteria for aneurysms in KD
 - 1.5 times the size of the adjacent normal segment
 - Diameter \geq 3 mm in a child < 5 yrs of age
 - Diameter \geq 4 mm in a child > 5 yrs
 - Small: < 5 mm Medium: 5 8 mm Giant: > 8 mm

Kawasaki Disease: Indications and Frequency of 2D Echo



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REVIEW ARTICLE

An update on Kawasaki disease II: Clinical features, diagnosis, treatment and outcomes

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Journal of Paediatrics and Child Health 49 (2013) 614-623 Royal Australasian College of Physicians

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Kawasaki Disease: Indications of 2D Echo

- The main aim of echocardiography is to assess the presence of coronary artery dilatation or aneurysm formation
- To check for the presence of valvular regurgitation, ventricular (dys)function or a pericardial effusion, suggestive of pericarditis and/or myocarditis

Yim, Curtis, Cheung, Burgner

Kawasaki Disease: Coronary Involvement

The main sites of coronary involvement (in order of decreasing frequency)

- proximal left anterior descending artery
- proximal right coronary artery
- left main coronary artery
- left circumflex branch
- distal right coronary artery
- the junction of the right and posterior descending coronary artery

Yim, Curtis, Cheung, Burgner

Kawasaki Disease: Frequency of 2D Echo

• All suspected cases of Kawasaki disease at initial presentation

Yim, Curtis, Cheung, Burgner

Echocardiogram is considered positive if any of 3 conditions are met:

- Z score of LAD or RCA \geq 2.5
- Coronary arteries meet Japanese Ministry of Health criteria for aneurysms
- ≥3 other suggestive features exist
 - perivascular brightness
 - lack of tapering
 - decreased LV function
 - mitral regurgitation
 - pericardial effusion,
 - -z scores in LAD or RCA of 2–2.5

VALVAR ABNORMALITIES

TR, MR, AR

- Mild, transient
- Secondary to valvulitis or myocarditis in the acute phase
- Aortic root dilation may cause aortic regurgitation



ACUTE, SEVERE AR

 Associated with myocardial ischemia and papillary muscle dysfunction

Myocardial Abnormalities

Decrease ventricular function

•Secondary to myocarditis during the acute phase

Abnormal regional wall motion

•Secondary to coronary artery abnormalities

Myocardial dysfunction/ mitral regurgitation

- Papillary muscle ischemia
- •Scarring

Pericardial Abnormalities

Pericardial Effusion

- Moderate amount
- Secondary to pericardial inflammation
- Increase risk of coronary artery changes
- Supportive data in "incomplete" KD



Fate of Coronary Aneurysm, JCS 2008

- Regression (30-50%)
- Localized stenosis (10-21 Y/O in 4-12 %)
- Occlusion

 Segmental stenosis (15%) Braid-like lesion Pericoronary communications Bridging vessels



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KD CAA Resolution

- Angiographic spontaneous resolution may occur in about 50% of CAA, especially in the small coronary aneurysms
- The size of the aneurysm is a factor in prognosis, with giant aneurysms (>8 mm) being associated with a higher risk of rupture, thrombosis and stenosis, which can cause myocardial infarct and death
- Giant aneurysms usually do not regress

6-8 WEEKS AFTER DIAGNOSIS Transient changes in coronary dilation and ectasia often resolves abnormalities Kawasaki Syndrome For chronic coronary artery High persistant fever-**2 WEEKS** Redness of the eyes abnomalities Enlarged lymph nodes Red, chapped, cracked lips & swelling of the neck Sore throat Appearance of loint nair ANNUAL cardiac **FOLLOW-UP** abnormalities Coronary Artery aneurysms leart muscle inflammation Swollen hands & feet, peeling

Recommendations for Follow-up Imaging

Diarrhea

skin on hands, palms,toes,

soles of feet

FOLLOW UP OF THE PATIENT: 2D ECHO (2 MONTHS AFTER DISCHARGE): (+) LEFT MAIN CORONARY ARTERY ANEURYSM 5.2 MM

CARDIAC EVALUATION

- Echocardiography : <u>BASELINE</u> and repeated at <u>two and six</u> weeks of illness to evaluate for CA involvement
- Children clinically well following IVIG therapy, have normal echo at two weeks SELDOM develop NEW abnormalities
- Those with CA aneurysms, or those at higher risk for them, warrant more FREQUENT echocardiograms
- Repeated clinical evaluations during the <u>FIRST ONE TO TWO</u> <u>MONTHS following diagnosis</u> of KD to detect arrhythmias, heart failure, valvular insufficiency or myocarditis

KD Follow-Up Recommendations

- The American Heart Association recommends performing trans- thoracic echocardiography at diagnosis, and then 2 weeks and 6–8 weeks after the initial illness for uncomplicated cases
- The timing of additional studies is case specific and is dictated by the severity of coronary artery involvement
- In general, individual cases should be discussed in consultation with a paediatric cardiologist
- Coronary aneurysms greater than 5 mm in size require close monitoring because of an elevated risk of developing stenotic lesions within the vessel

KAWASAKI DISEASE:

Complex Coronary Artery Abnormalities

Giant coronary artery aneurysm for surveillance of thrombus formation

- At least twice per week
- Once weekly on the 1st 45 days of illness
- Monthly until the 3rd month of the disease
- Once every 3 months until the end of the 1st year of illness

RATIONALE FOR IMAGING

- Accurate assessment of coronary artery morphology
- Identify and characterize abnormality (aneurysm or stenosis)
- Risk stratification and therapeutic management
- Long-term follow-up into adult life is needed
 - Abnormal vascular morphology and function persists despite regression of aneurysms
 - New lesions have been found in 3% up to 20 years after the initial diagnosis
 - About 4% of children eventually develop ischemic heart disease

CORONARY ARTERY IMAGING

- Echocardiogram
 - Non invasive test, first line screening
 - Anatomical & physiologic parameters
 - More difficult as the child grows and body size increases
 - Visualization of the mid to distal segments can be limited
- Selective coronary angiography / conventional angiogram
 - Gold standard for the evaluation of a coronary lesions
 - Invasive nature, radiation exposure, contrast
 - Not generally accepted as a routine follow-up
 - Low level of acceptance by parents

CORONARY CT ANGIOGRAPHY



OBJECTIVES

1. To discuss the indications for doing 2-D Echo in a patient with Kawasaki Disease and how often should it be done.

2. If a patient is allergic to aspirin, to discuss other alternative drugs.

3. To discuss the duration of treatment, with or without aneurysm.

CORONARY ARTERY DISEASE

- Larger aneurysms are at risk of developing stenosis
- Severe stenotic lesions or giant aneurysms are often associated with calcification
- Occluded segments may have recanalized collaterals
- Potential life-threatening event such as myocardial infarction

Cardiac Related Treatment in KD

- Anti-thrombotic
- Aspirin alternative
- Supports
- Statin

Table 15 Antiplatelet drugs and anticoagulant drugs

Drug	Dose	Adverse drug reactions (ADRs) and precautions	
acetylsalicylic acid (Bufferin or Bayaspirin)	30 to 50 mg/kg divided into 3 doses during the acute phase, 3 to 5 mg/kg once daily after defervescence	Hepatic function disorder, gastrointestinal ulcer, Reye syndrome (higher incidence at ≥40 mg/kg), bronchial asthma Use other drugs during varicellainfection and influenza.	
Flurbiprofen (Froben)	3 to 5 mg/kg, divided into 3 doses	Hepatic function disorder, gastrointestinal ulcer Use when severe hepatic disorder due to aspirin develops.	
Dipyridamole (Persantin, Anginal)	2 to 5 mg/kg, divided into 3 doses	May induce angina in patients with severe coronary stenosis. Coronary steal phenomenon, headache, dizziness, thrombocytopenia, hypersensitivity, dyspepsia	
Ticlopidine (Panaldine)	5 to 7 mg/kg, divided into 2 doses	Thrombotic thrombocytopenic purpura (TTP), leukopenia (granulocytopenia), serious hepatic function disorder Blood tests must be performed every other week during the first 2 months of treatment.	
Clopidogrel (Plavix)	1 mg/kg, once daily	TTP, gastrointestinal symptoms, malaise, myalgia, headache, rash, purpura, pruritus Bleeding tendency may develop when used with aspirin.	
Unfractionated heparin (IV) Low-molecular-weight heparin (SC)	Loading dose 50 units/kg, maintenance dose 20 units/kg to maintain an APTT of 60 to 85 sec (1.5 to 2.5 times baseline) • Infants <12 months of age Treatment: 3 mg/kg/day, divided into 2 doses (every 12 hours) Prevention: 1.5 mg/kg/day, as above • Children/adolescents Treatment: 2 mg/kg/day, divided into 2 doses (every 12 hours) Prevention: 1 mg/kg/day, as above	Major ADRs: Shock/anaphylactoid reaction, bleeding, thrombocytopenia, thrombocytopenia/ thrombosis associated with heparin-induced thrombocytopenia (HIT)	
Warfarin (Warfarin)	0.05 to 0.12 mg/kg, once daily (0.05 to 0.34 mg/kg/day in the AHA guidelines) 3 to 7 days required to obtain efficacy	Dose should be adjusted to an INR of 1.6 to 2.5 (2.0 to 2.5 in the AHA guidelines) and a thrombotest (TT) value of 10 to 25%. Sensitivity to this drug, hepatic function disorder, and bleeding ADRs are possible.	

KD Duration of Treatment

ACUTE PHASE

 Low-dose aspirin is continued for at least the first 6–8 weeks of the illness, during which time the risk of coronary artery damage is greatest.

CONVALESCENT PHASE

- IF the ECHO of THE CAA is normal at 6–8 weeks, the aspirin is usually discontinued.
- If mild coronary artery dilatation or small to medium aneurysm(s) (>3 and <6 mm diameter) remain after this period, aspirin should generally be continued until resolution of arterial involvement is documented
- Addition of clopidogrel, dipyridamole or low molecular weight heparin may be considered if coronary artery aneurysm(s) enlarge.
- Warfarin is recommended if giant aneurysms (>8 mm diameter) are present.
 Yim, Curtis, Cheung, Burgner

KD Duration of Treatment

Non-responders to IVIG

- Approximately 10–15% of Kawasaki disease patients have a persistent or recrudescent fever more than 36 h after the end of the initial IVIG infusion and require further treatment
- A variety of risk factors both before IVIG therapy and immediately following therapy have been associated with lack of response to IVIG, including initial IVIG treatment before day 5 of illness, a recurrent episode of Kawasaki disease, male sex, a low platelet count and elevated alanine transaminase (ALT) and CRP levels.
- Those not responding to IVIG have an increased risk of coronary artery aneurysms, especially giant aneurysms
 ^{Yin, Curtis, Cheung, Burgner} Update on Kawasaki disease: Epidemiology, aetiology

KD Duration of Treatment

- A multi-centre retrospective study of warfarin and aspirin combination therapy in Kawasaki disease patients with giant coronary aneurysms
- High cardiac event-free survival with an increased risk of haemorrhagic complications

Kenji Suda et al Multicenter and Retrospective Case Study of Warfarin and Aspirin Combination Therapy in Patients With Giant Coronary Aneurysms Caused by Kawasaki Disease Pediatric Cardiology and Adult Congenital Heart Disease *Circ J* 2009; **73**: 1319 – 1323

CARDIAC EVALUATION

- Electrocardiogram (ECG)
- Stress Testing
- Coronary Angiography
- Serum Lipid Profiles

Kawasaki Disease: Dyslipidemia

- Dyslipidaemia is common in acute Kawasaki disease
- With a pro-atherosclerotic profile (i.e. increased low density lipoprotein (LDL) and decreased high density lipoprotein (HDL))
- Whether these lipid abnormalities persist or are important in longer term cardiovascular risk remains unclear

Yim, Curtis, Cheung, Burgner

Dyslipidemia in KD

Noto quoted by Duarte et al:

 Demonstrated that patients with a history of KD have long- term structural and functional alterations that increase the propensity towards subclinical atherosclerosis with age

> Insights Imaging. 2010 Sep; 1(4): 223–231. Published online 2010 Jul 30

ATHEROSCLEROTIC CORONARY DISEASE

- > 2 years old screened for dyslipidemia
- fasting lipid profile (HDL, LDL)
- Check cholesterol ONE YEAR after the acute phase of the disease
- If results are normal repeat every five years

RISK LEVEL	THERAPY	PHYSICAL ACTIVITY	FOLLOW-UP	INVASIVE TESTING			
l (no coronary artery changes)	None beyond first 6-8 weeks	No restrictions beyond first 6-8 weeks	Counseling at 5-year- intervals	None			
II (transient coronary artery ectasia)	None beyond first 6-8 weeks	No restrictions beyond first 6-8 weeks	Counseling at 3-to-5-year intervals	None			
III (one small medium coronary artery aneurysm)	Low-dose aspirin at least until aneurysm regression is documented	For patients < 11 years: no restrictions;for patients of 11-20 years: physical activity must be guided by stress test and myocardial perfusion scan; discouraged contact or high-impact sports	Annual echocardiogram + ECG; biannual stress test and myocardial perfusion scan	Angiography, if non invasive tests suggest ischemia			
				1			
IV (≥1 large or giant coronary artery aneurysm or multiple aneurysms without obstruction)	Long term antiplatelet therapy and warfarin or low molecular weight heparin	Contact or high-impact sports should be avoided because of risk of bleeding; other physical activity recommendations must be guided by stress test and myocardial perfusion scan	Biannual echocardiogram + ECG; annual stress test and myocardial perfusion scan	Angiography at 6-12 months after the disease			
V (coronary artery obstruction)	Long term low-dose aspirin, warfarin or low molecular weight heparin if giant aneurysms persist	Contact or high-impact sports should be avoided because of risk of bleeding; other physical activity recommendations must be guided by stress test and myocardial perfusion scan	Biannual echocardiogram + ECG; annual stress test and myocardial perfusion scan	Angiography is recommended to address the best personalized therapeutic option			



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"Take Good Care of My Heart" <3