Kawasaki Disease and Exercise

Indexing Metadata/Description

› Title/condition: Kawasaki Disease and Exercise
› Synonyms: Exercise and Kawasaki disease; Kawasaki syndrome and exercise; infantile polyarteritis and exercise; exercise and infantile polyarteritis; mucocutaneous lymph node syndrome and exercise; lymph node syndrome, mucocutaneous and exercise; exercise and mucocutaneous lymph node syndrome
› Anatomical location/body part affected: Heart/coronary arteries (other muscular arteries may also be affected); skin, eyes, lips and oral cavity, hands and feet, neck, and lymph nodes are involved in the acute inflammatory phase
› Area(s) of specialty: Cardiac rehabilitation, pediatric rehabilitation
› Description

• Kawasaki disease (KD) is a self-limiting episode of generalized vasculitis in childhood. Patients are more often Asian and under 5 years of age. The etiology is unknown. Symptoms include a short period of fever (about 10 days), bilateral nonexudative conjunctivitis, erythema of the lips and oral mucosa, rash, and cervical lymphadenopathy(1)

• Incidence of KD is highest in the Japanese population, at 243.1-264.8 per 100,000. Incidence is reported to be 8.39/100,000 in the UK, 22.5/100,000 in white Californians, 29.8/100,000 in the black population, and 50.4/100,000 in Asian and Pacific Islanders(21)

• KD is the leading cause of acquired pediatric heart disease in North America, Europe, and Japan.(22) It is also increasing in countries that are rapidly becoming industrialized, such as China and India(22)

• After the acute stage resolves, 15% to 25% of children not treated with intravenous immunoglobulin (IVIG) develop coronary artery abnormalities (e.g., arteritis and aneurysms) that might lead to ischemic heart disease, myocardial infarction, or sudden death(1,2)

• The long-term cardiac sequelae of KD can remain undiagnosed for years. For example, in 74 persons with a history of KD, the mean age at presentation with serious cardiac symptoms was 24.7 +/- 8.4 years (range, 12 to 39 years)(3)

• Myocardial perfusion defects on exercise testing were found in 25/46 (54%) of children and adolescents with a history of KD, including 37% of those having no objective evidence of coronary artery lesions, 63% of those with resolved aneurysms, and 100% of those with persistent coronary aneurysms(4)

• Exercise-inducible myocardial ischemia is common in the subset of patients with KD with persistent coronary artery aneurysms and/or stenosis(2)

• Myocardial injury due to repeated small-vessel thrombosis was found on cardiac biopsy several years after acute KD in 16 patients (aged 5 to 16 years) with giant coronary aneurysms(6)

• Post-KD patients with persistent coronary artery lesions and/or aneurysms represent a special cardiac population at risk for potentially life-threatening events.(1,2) Children and adults with a history of KD who present for physical therapy should be considered
to be at high risk for exercise-inducible coronary artery insufficiency even though most remain asymptomatic.\(^{(1,5)}\)

- There are no established cardiology guidelines for the evaluation and treatment of patients who have had KD\(^{(7)}\)

**ICD-9 code:** 446.1 Kawasaki disease, acute febrile mucocutaneous lymph node syndrome

**ICD-10 code:** M30.3 mucocutaneous lymph node syndrome (Kawasaki)

(ICD codes are provided for the reader’s reference, not for billing purposes)

**Reimbursement:** Reimbursement for therapy will depend on insurance contract coverage; no specific issues or information regarding reimbursement have been identified

**Presentation/signs and symptoms**

- Pediatric or adult patient with a history of KD
- Presentation for cardiac rehabilitation exercise training or referred for treatment of an unrelated condition for which exercise therapy is indicated
- Normal physical functioning
- Usually asymptomatic with normal exercise tolerance for age\(^{(4)}\)

  - In a case report, an athletic previously healthy teenage boy collapsed at school after cross-country practice. Subsequent evaluation provided retrospective evidence that a remote history of presumed viral hepatitis was actually KD\(^{(19)}\)

  - The patient had recovered from the acute illness with no apparent effects and returned to his normal activities until the sudden cardiac death and resuscitation event
  - Extensive coronary artery abnormalities were found on cardiac catheterization

- Possibly abnormal resting electrocardiogram (ECG)\(^{(8)}\)
- Abnormal cardiac radionuclide or 2-dimensional echocardiographic exercise study, if conducted

**Causes, Pathogenesis, & Risk Factors**

**Causes**

- The exact etiology of KD is unknown\(^{(9)}\)
- Several infectious agents (New Haven coronavirus, parvovirus, bocavirus, cytomegalovirus, *Yersinia pseudotuberculosis*, meningococcus), as well as bacterial superantigens and components of the immune system (interleukin 10 and 18), are implicated\(^{(1,7)}\)
- KD is not communicable\(^{(1,2)}\)

**Pathogenesis**

- Acute KD damages the media of the coronary artery wall. This often leads to one or more lesions and aneurysms\(^{(1,2)}\)
- Administration of IVIG within 10 days of the acute episode of KD appears to regulate the immune response, and in most cases the vasculitis resolves\(^{(1,5,7,8)}\)
- Aneurysms (especially giant ones) are associated with thrombosis and thrombotic occlusion. In addition, obstructive stenosis may develop over time in residual coronary artery lesions due to atherosclerosis\(^{(1,2,5,10)}\)
- Stenotic lesions that grow to narrow the luminal diameter more than 70% compromise the increase in coronary artery blood flow during periods of greater myocardial oxygen (O2) demand\(^{(4,11)}\)
- Major determinants of increased myocardial O2 demand during exercise are heart rate (HR), left ventricular systolic pressure (indexed by systolic blood pressure [SBP]), left ventricular wall tension, and myocardial contractility\(^{(11)}\)
- The product of HR x SBP (“rate-pressure product”) is a useful correlate of myocardial O2 demand; that is, as HR x SBP increases with exercise, myocardial O2 demand increases\(^{(12)}\)
- Exercise therefore increases the likelihood of transient myocardial hypoxia in post-KD patients with persistent coronary lesions\(^{(5)}\)
- Exercise-inducible myocardial perfusion defects are common in post-KD patients with coronary aneurysms and have been imaged with radionuclide (e.g., thallium-201 or technetium-99m)scintigraphy\(^{(4,11)}\) and stress echocardiography\(^{(13)}\)
- Authors of a study in Canada found significantly more myocardial perfusion defects on treadmill exercise testing in post-KD children and adolescents with a history of coronary aneurysms (n = 133) than controls without (n = 117). However, HR, SBP, and diastolic BP responses, as well as endurance time, were similar between the groups\(^{(20)}\)
Abnormal ventricular wall motion on stress testing has also been noted using radionuclide imaging in asymptomatic post-KD patients. The prescribed intensity of therapeutic aerobic exercise should, therefore, not exceed the patient’s ischemic threshold. This can be achieved by maintaining HR x SBP below that associated with the onset of cardiac ischemia observed on stress imaging.

If exercise-induced myocardial hypoxia becomes extensive, SBP may fall because of left ventricular wall motion dysfunction (indicated on exercise echocardiography or radionuclide imaging). Exercise should be stopped if SBP falls 10 mm Hg or more below the baseline SBP.

Limiting exercise intensity to below the ischemic HR x SBP is important because most KD patients with exercise-inducible myocardial hypoxia do not experience angina pectoris or other symptoms of cardiac ischemia. Consequently, they have no internal feedback to know when their ischemic threshold is exceeded during exercise.

Some post-KD patients with a totally occluded coronary artery also remain asymptomatic during exercise, perhaps because collateral vessels maintain some myocardial flow around the blockage.

Risk factors
- Genetically susceptible children (especially Asian or Pacific Islanders)
- Of 50 patients (ages 18 to 69) with a history of KD and acute coronary syndrome, 43 (86%) were male and 7 (14%) were female
- Residual giant aneurysm
- Smoking
- Children with a history of allergic diseases are at increased risk of KD
- Advanced maternal age
- Hospitalization in early infancy
- Pregnant women with a history of KD have an increased risk of complications during pregnancy and of KD in their children

Overall Contraindications/Precautions
- In pediatric cases, obtain written referral with exercise restrictions from treating physician
- In pediatric cases, obtain written consent from parent or legal caretaker
- Absolute contraindications to exercise
  - Acute systemic illness or fever
  - Chest pain or shortness of breath at rest
  - Resting SBP greater than 200 mm Hg or resting diastolic BP (DBP) greater than 110 mm Hg
  - Orthostatic fall in SBP with symptoms
  - Critical aortic stenosis
  - Uncontrolled atrial or ventricular arrhythmias
  - Uncontrolled sinus tachycardia greater than 120 beats/min
  - Uncompensated congestive heart failure
  - 3rd-degree atrioventricular block without pacemaker
  - Active pericarditis or myocarditis
  - Recent embolism
  - Thrombophlebitis
  - Uncontrolled diabetes
  - Severe orthopedic conditions that would restrict exercise
  - Uncontrolled metabolic conditions such as acute thyroiditis, hypokalemia, hyperkalemia, hypovolemia, etc.
- General cardiac rehabilitation guidelines should be followed because patients with KD with persistent coronary artery defects are at high risk for cardiac sequelae at any age.
- Stop exercise and notify physician if patient reports symptoms of coronary insufficiency such as angina, inappropriate shortness of breath, dizziness, etc.
In the absence of exertion-related symptoms, exercise testing or training should be terminated at the predetermined ischemic threshold specific for the patient. See specific Precautions/recommendations under Examination and Contraindications/precautions under Assessment/Plan of Care.

### Examination

#### Precautions/recommendations

If available, obtain results of recent exercise stress test with radionuclide or echocardiographic imaging. Identify HR x SBP associated with any perfusion defects or wall motion changes. Do not exceed: 1) this rate-pressure product during assessment of functional capacity or during exercise therapy, or 2) the physician’s restrictions for exercise intensity.

#### History

**History of present condition:** Document date and age of treatment for KD. Is the patient physically active, and are any adverse symptoms related to exercise? If available, what were the results of exercise stress testing with radionuclide (e.g., thallium or technetium) imaging or cardiac ultrasound?

**Course of treatment**

- **Medical management:** During the acute stage of KD most patients receive IV immunoglobulins and aspirin. Some also receive steroid therapy. Has the patient been treated for myocardial infarction, arrhythmias, atrioventricular block, or other heart conditions? Is the patient following a cardiac risk factor reduction program, such as smoking cessation, dietary restriction, weight loss, or prescribed exercise?

- **Operative management:** Document date and reason for any cardiac surgical procedure that has been performed. Is the patient receiving ongoing postoperative care?

- **Surgical management** may include interventional catheterization, coronary angioplasty, stent placement, or coronary artery bypass graft surgery.

- **Medications for this condition:** Obtain a complete list of prescribed cardiac and other medications that are currently being taken.

- **Diagnostic tests completed:** Document the results of laboratory tests related to exercise, including noninvasive cardiac stress testing (standard 12-lead ECG, echocardiography, radionuclide scans), coronary angiography, etc.

- **Home remedies/alternative therapies:** Document any treatment at home or alternative therapies (e.g., acupuncture) that were tried and whether they helped or not.

- **Previous therapy:** Has the patient previously received therapeutic exercise and, if so, what specific exercise program was helpful or not helpful?

#### Aggravating/easing factors

If applicable, document activities that provoke symptoms and the methods used to relieve them.

- **Body chart:** Use a body chart to identify location of symptoms.

- **Nature of symptoms:** Ask the patient to describe the nature of reproducible symptoms.

- **Rating of symptoms:** Use a visual analog scale (VAS) or 0-10 scale to assess symptoms at their best (usually zero), worst, and at present. Use the Borg Rating of Perceived Exertion (RPE) Scale or other scale to estimate intensity of exertion.

- **Pattern of symptoms:** Are symptoms related to time of day, possibly in relation to time that medications are taken? Also, document changes in symptoms due to weather or other external variables.

- **Sleep disturbance:** Does the patient complain of nocturnal symptoms? If present, document the usual number of wakings/night and report this to physician.

- **Other symptoms:** Document other symptoms that increase disability in ADLs and/or indicate need for medical consultation.

- **Respiratory status:** Is there a history of respiratory compromise?

- **Barriers to learning**

  - Are there any barriers to learning? Yes __ No __

  - If Yes, describe (e.g., cognitive impairment, speech deficit, foreign language)

#### Medical history

- **Past medical history**

  - **Previous history:** What was the patient’s heart health history (e.g., myocardial infarction, cardiac arrhythmia) prior to this referral?
- **Comorbid diagnoses:** Ask the patient about coexisting problems, including diabetes, cancer, musculoskeletal disorders, psychiatric disorders, chronic lung disease, etc.

- **Medications previously prescribed:** Obtain a comprehensive list of medications (including over-the-counter drugs) taken for other health problems such as diabetes or asthma

- **Other symptoms:** Ask about other symptoms that have affected the patient’s mobility in ADLs

- **Social/occupational history**
  - **Patient’s goals:** Document patient’s and parent or caregiver’s expectations/goals for outcomes after treatment. What social or occupational roles does the patient expect treatment will improve?
  - **Vocation/avocation and associated repetitive behaviors:** Does the patient work or attend school? Is the patient currently on work disability? Did the patient participate in vigorous -recreational activities or sports prior to this referral? How much daily physical activity does the patient typically do?
  - **Functional limitations/assistance with ADLs/adaptive equipment:** Document assistive devices that are being used (e.g., cane, crutches, walker or wheelchair)
  - **Living environment:** Identify barriers to mobility in the home (e.g., stairs, number of floors in home, lack of caregivers) and whether any modifications are necessary. What support system (family/caregiver) is available?

- **Relevant tests and measures:** (While tests and measures are listed in alphabetical order, sequencing should be appropriate to patient medical condition, functional status, and setting)
  - **Anthropometric characteristics:** Determine height, weight, and body mass index (BMI)
  - **Assistive and adaptive devices:** Is an assistive device (AD) used for ambulation? Is it an appropriate choice of AD? Is it being used correctly?
  - **Balance:** Assure that static and dynamic balance reactions are appropriate for use of exercise equipment such as treadmill or elliptical trainer. Perform appropriate balance measure such as Berg Balance Scale or Functional Reach Test
  - **Cardiorespiratory function and endurance:** Assess HR, BP, and breathing frequency during activity and quiet rest. The 6-minute walk for distance test (6MWT) can be used to assess cardiorespiratory functional capacity
  - **Circulation:** Assure that peripheral pulses are present in all limbs
  - **Functional mobility:** Assure normalcy in gross movement during transfers and functional tasks using the upper extremities (e.g., reaching, pulling, pushing, holding) and lower extremities (e.g., steps, squatting, kneeling, kicking). FIM or WeeFIM may be used
  - **Gait/locomotion:** Prior to prescribing a walking or jogging exercise program, assure that ambulatory function is normal, including synchrony of limb movements as well as posture, and that safe limits can be followed
  - **Muscle strength:** Manually scan strength in functional tasks (e.g., handgrip, pushing, pulling, sit-up, squatting). Assess strength using manual muscle testing (MMT), dynamometry, or weights in muscle groups targeted for exercise training
  - **Neurodevelopmental development:** Assess as indicated in children who have not met developmental milestones
  - **Observation/inspection/palpation:** Assess for any physical deformities that might prevent or restrict participation in the prescribed exercise program
  - **Pain/tenderness/fatigue:** Assess for general pain, tenderness, and fatigue in limbs during or after exercise testing
  - **Range of motion:** Assess for functional ROM in all extremities during the prescribed exercise
  - **Reflexes:** Assess deep tendon reflexes
  - **Sensation:** Scan dermatomes for normal sensation
  - **Special tests**
    - In compliance with medical guidelines, in exercise testing on a treadmill or cycle ergometer to the end point predetermined by the referring physician

**Assessment/Plan of Care**

- **Contraindications/precautions**
  - **Assure close supervision with instruction during the exercise training sessions**
  - **Monitor BP on a regular basis during exercise.** According to standard exercise guidelines, exercise testing or exercise training should be terminated if
    - SBP exceeds 260 mm Hg or DBP exceeds 115 mm Hg
    - SBP fails to rise more than 20 mm Hg
    - SBP falls more than 10 mm Hg
  - Exertional symptoms such as chest discomfort, lightheadedness, or dyspnea suggest cardiac insufficiency
• Resting BP higher than 180/110 mm Hg is an absolute contraindication and resting BP higher than 160/100 mm Hg is a relative contraindication for resistance exercise\(^{(12,16)}\)

• To prevent an exaggerated BP response to exercise, provide the patient with a thorough orientation to using the prescribed exercise equipment and with adequate warm-up time

• To make the exercise safe for either aerobic or resistance training, monitor HR and BP for appropriate responses and the reported perceived exertion and/or symptoms

• Extend the cool-down period to avoid having the patient stop suddenly after exercise as this may cause a precipitous fall in SBP, leading to orthostatic hypotension and possibly syncope due to venous pooling

• Clinicians should follow the exercise guidelines of their clinic/hospital and what is ordered by the patient’s physician

**Diagnosis/need for treatment:** History of KD/referral for supervised exercise training or treatment that may include exercise therapy

**Differential diagnosis:** Scarlet fever, Stevens-Johnson syndrome, measles, Rocky Mountain spotted fever, infectious mononucleosis, juvenile rheumatoid arthritis

**Prognosis:** Long term prognosis for adults with history of KD but without coronary artery aneurysms is excellent\(^{(7)}\)

Prognosis for patients with a history of cardiac complications requires regular follow up with transthoracic echocardiography and depends on risk stratification\(^{(7)}\)

• Coronary artery aneurysms occur in 15%-25% of untreated patients; 2%-3% of untreated patients die as a result of coronary vasculitis\(^{(21)}\)

• As more children with a history of KD reach adulthood, more studies are needed to improve the understanding of the long-term cardiovascular sequelae\(^{(21)}\)

• In patients with giant (> 8mm) coronary artery aneurysms, a 30 year survival of 88% has been reported, with a 16% myocardial infarction rate and 59% requiring revascularization within a 25 year follow-up\(^{(23)}\)

• Many patients with coronary artery aneurysms undergo regression of aneurysmal dilatation; however, the coronaries remain abnormally thickened and vessel wall calcification often occurs\(^{(21)}\)

**Referral to other disciplines:** Cardiologist for consultation

**Other considerations**

• Randomized controlled trials as well as specific guidelines for exercise are lacking

• Published research on exercise training in KD is limited to a pilot study that combined 10 to 12 days of cycle exercise with intravenous heparin in 7 patients with stress-induced myocardial ischemia\(^{(15)}\)

• No studies of resistance exercise training were found in the literature

• Because of the increased risk of myocardial ischemia/infarction, exercise guidelines for cardiac patients should be followed\(^{(12,16)}\)

• Patients at risk because of persistent aneurysms and/or coronary lesions will nevertheless likely remain asymptomatic during exercise. However, exercise restrictions should be obtained from the referring physician and, if available, based on preliminary exercise studies using radionuclide or echocardiographic myocardial imaging techniques

• Similar to all athletes with known coronary artery disease, athletes with a history of KD should undergo maximal treadmill or bicycle exercise testing, preferably with myocardial imaging, to assess their exercise tolerance and safe cardiovascular limits. They should be informed that the risk of a cardiac event is increased in competitive sports, and may have to restrict their participation to low-intensity competitive sports\(^{(17)}\)

**Treatment summary**

**Aerobic exercise training**

– Type of activity: Rhythmic movement with the legs (e.g., walking, jogging, or cycling), arms (e.g., upper-body cycle ergometer), or both legs and arms (e.g., elliptical trainer with arm levers)

– Intensity: Provided there are no contraindications, “light” to “somewhat hard” exertion, equaling 11 to 13 on the Borg RPE Scale (6-to-20).\(^{(18)}\) Do not exceed the HR x SBP associated with any perfusion defects or wall motion changes on exercise imaging studies

– Duration: Continuous or discontinuous exercise totaling 30 min of physical activity per day. For overweight patients, 5 hours or more per week to promote weight loss

– Frequency: 3 alternating days per week

**Resistance exercise training**

– Target areas of muscle weakness
– Type of activity: Circuit training. Weight-lifting exercises on machines or using free weights (e.g., leg press, chest press, leg extension, lat pull-down, leg curls, shoulder press, biceps curl, triceps press)
– Intensity: Low to moderate intensity. Resistance training at 40-60% of 1-RM is considered safe and effective in persons with cardiovascular disease (16)
– Duration: 1-3 sets of 10 repetitions per exercise, taking about 30 min to complete the exercise session
– Frequency: 2-3 nonconsecutive days per week

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<th>Intervention</th>
<th>Expected Progression</th>
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<tr>
<td>Reduced strength, aerobic endurance, and functional capacity in a patient with high risk of exercise-inducible cardiac ischemia</td>
<td>Safe improvement of fitness to age-norm or better</td>
<td><strong>Exercise therapy</strong>&lt;br&gt;See review in <em>Treatment summary</em>, above, for: Aerobic exercise. Resistance exercise&lt;br&gt;Maintain exercise intensity within safe limits for patient</td>
<td>As fitness improves, gradually progress the intensity and duration of exercises to the maintenance phase</td>
<td>Provide the patient with an individualized home program at discharge from supervised exercise</td>
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**Desired Outcomes/Outcome Measures**

› Improved aerobic endurance  
  • Aerobic fitness assessed by cycle or treadmill graded exercise testing
› Improved strength  
  • Strength assessed by MMT, with machines, or using free weights
› Improved functional exercise capacity in ADLs  
  • Physical functioning assessed by 6MWT
› Improved quality of life  
  • SF-36 Health Status Questionnaire (physical functioning scale and physical composite scale)

**Maintenance or Prevention**

› Primary prevention of KD is difficult, as its etiology remains unclear (2) Secondary prevention of complications may include  
  • Continue prescribed exercise training through independent home program  
  • Weight reduction and control, as indicated  
  • Dietary program, as prescribed  
  • Aspirin therapy in patients who develop coronary aneurysm (2)  
  • A heart-healthy lifestyle is essential for adults with history of KD, even those without coronary artery complications (2)  
  – Persistence of subclinical vasculitis has been found in a subset of patients and may place them at higher risk for cardiovascular events (21)

**Patient Education**

› Web site for the Kawasaki Disease Foundation, [http://www.kdfoundation.org/](http://www.kdfoundation.org/)
**References**


10. Tsuda E, Abe T, Tamaki W. Acute coronary syndrome in adult patients with coronary artery lesions caused by Kawasaki disease: a review of case reports. *Cardiol Young*. 2011;21(1):74-82. (R)


