Update on Kawasaki Disease
Cardiovascular Complications

KAAP Progress in Pediatrics Spring 2019

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- I have no relevant financial relationships with the manufacturers(s) of any commercial products(s) and/or provider of commercial services discussed in this CME activity
- I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation
Outline

- Review the cardiac findings, acute and long term cardiovascular complications of Kawasaki disease (KD)
- Treatment of acute manifestations
- Long term follow up and surveillance
- Highlight recommendations in the new AHA guidelines

Guideline

KD and CVD

- KD is the most common cause of acquired heart disease in children in developed countries
- Untreated coronary aneurysms occur in 25%, ~4% with timely initiation of IVIG treatment
- Mortality occurs from coronary thromboses and myocardial ischemia - peak mortality occurs between 15-45 days after onset of fever
- Hospital mortality ~0.17%, mortality > in children > 10 yr (1.4% vs 0.11%)


- SMR beyond acute illness elevated for all patients with cardiac sequelae (SMR, 1.86; 95% confidence interval, 1.02–3.13)


- Sudden death /MI can occur from missed KD
- 5% of adults with MI < 40 yr had lesions of KD

Cardiac Involvement in KD

- Myocardial inflammation ~ 50-70% patients
- Myocarditis occurs early and is transient
- ~25% have mitral regurgitation (mild-moderate)
- Aortic regurgitation is rare ~ 1%, may be related to aortic dilation
- Aortic root dilation ~ 10%
- Other arterial abnormalities – aneurysms/thrombosis/rupture- axillary, subclavian, brachial, femoral A.
- Peripheral gangrene

Coronary Arteries in KD

Ref: AHA guideline Circulation 2017
Coronaries in KD

- Range from dilation to giant aneurysms
- Proximal coronary segments
- Transient dilation (Z score < 2.5) most common, resolves in 4-8 weeks
- 30-50% patients – dimensions in normal range but decrease with follow up
- Giant/large aneurysms asymptomatic unless causing ischemia – difficult recognition in infants, rarely rupture causing tamponade

Clinical findings

- Tachycardia
- Hyperdynamic precordium
- Murmur- systolic ejection murmur, mitral regurgitation, aortic regurgitation
  - 25% incidence of valvulitis (mitral valve)
- Gallop – myocardial inflammation and edema
- Pericardial rub- pericarditis
- 5% - cardiovascular collapse (KD shock syndrome)
Electrocardiogram

- Prolonged PR
- ST- T wave changes
- Low voltage complexes (myocarditis)
- Ischemia
- Malignant arrhythmia

Echocardiography

- Mainstay of cardiac imaging in KD
- Soon after diagnosis, but treatment should not be delayed
- Consider sedation (<3yrs, irritable child)
- If initial quality poor, repeat sedated echo in 48 hrs
- Initial echo in first week of illness- normal
- Guideline specifies standards of imaging including equipment and imaging protocol
Classification of Coronary Anomalies

Based on Z scores, not absolute dimensions

Z-Score Classification

1. No involvement: Always <2
2. Dilation only: 2 to <2.5; or if initially <2, a decrease in Z score during follow-up ≥1
3. Small aneurysm: ≥2.5 to <5
4. Medium aneurysm: ≥5 to <10, and absolute dimension <8 mm
5. Large or giant aneurysm: ≥10, or absolute dimension ≥8 mm

When to echo?

- At diagnosis
- Uncomplicated patients – 1-2 weeks, 4-6 weeks
- Evolving coronary artery abnormalities (Z score >2.5)- 2/week till progression stops
- Large or giant aneurysms- 2/week during expansion, 1/week in the first 45 days of illness, and then 1/month for 3 months
Limitations of Echo

- Difficult to detect thrombosis and stenosis
- Body size, acoustic windows
- Calcification can affect visualization
- Distal segments difficult to visualize
- CT angiography, CMR, invasive angiography

Acute Management

- Prevention and treatment of thrombosis
- Adjustment of anti-thrombotic therapy for evolving aneurysms
- Influenza vaccine to patients > 6 months/ family members
- Varicella vaccine – consider alternate antiplatelet agent for 6 weeks
Thrombosis Prevention

- Low dose aspirin (ASA) 3-5 mg/kg/day for 4-6 weeks after onset of illness
- Rapidly expanding or giant aneurysms (Z score > 10) - add warfarin /LMWH for systemic anticoagulation
- Risk for thrombosis (aneurysms > 8mm, > 10 Z score, history of thrombosis) – triple therapy
- Ibuprofen and other NSAID’s should be avoided

Thrombosis Treatment

- Thrombolytic therapy – tPA
- Mechanical restoration of lumen at cardiac catheterization
- Monitor for bleeding
- Low dose thrombolytic + glycoprotein IIb/IIIa inhibitor (abciximab) for large thrombus burden
Long term outcomes

- Coronary artery events (thrombosis, stenosis, intervention, MI, death) linked to severity of initial coronary disease and progression
- 16 year follow up
  - Z score <10 and dimension <8 mm : 1%
  - Z score ≥10 but absolute dimension <8 mm : 29%
  - Z score ≥10 and an absolute dimension ≥8 mm : 48%
- Giant aneurysms unlikely to regress

Risk Stratification

<table>
<thead>
<tr>
<th>Classification</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No involvement at any timepoint (Z score always &lt;2)</td>
</tr>
<tr>
<td>2</td>
<td>Dilation only (Z score 2 to &lt;2.5)</td>
</tr>
<tr>
<td>3</td>
<td>Small aneurysm (Z score ≥2.5 to &lt;5)</td>
</tr>
<tr>
<td>3.1</td>
<td>Current or persistent</td>
</tr>
<tr>
<td>3.2</td>
<td>Decreased to dilation only or normal luminal dimension</td>
</tr>
<tr>
<td>4</td>
<td>Medium aneurysm (Z score ≥5 to &lt;10, and absolute dimension &lt;8 mm)</td>
</tr>
<tr>
<td>4.1</td>
<td>Current or persistent</td>
</tr>
<tr>
<td>4.2</td>
<td>Decreased to small aneurysm</td>
</tr>
<tr>
<td>4.3</td>
<td>Decreased to dilation only or normal luminal dimension</td>
</tr>
<tr>
<td>5</td>
<td>Large and giant aneurysm (Z score ≥10, or absolute dimension ≥8 mm)</td>
</tr>
<tr>
<td>5.1</td>
<td>Current or persistent</td>
</tr>
<tr>
<td>5.2</td>
<td>Decreased to medium aneurysm</td>
</tr>
<tr>
<td>5.3</td>
<td>Decreased to small aneurysm</td>
</tr>
<tr>
<td>5.4</td>
<td>Decreased to dilation only or normal luminal dimension</td>
</tr>
</tbody>
</table>
Long term management

- Begins 4-6 weeks post onset
- Preventing thrombosis and myocardial ischemia
- Surveillance for coronary disease and inducible ischemia
- Promotion of optimal cardiovascular health – life style modification, prevention of risk factors for atherosclerosis

Primary Provider Role

- **Who should follow up with cardiologist?**
  - Level 1- discharge after 4 weeks – 12mo
  - Level 2- discharge after 12 mo, 3-5 yrs if dilation persists
  - Level 3-5 – cardiology follow up needed
Primary Provider Role

- Cardiovascular risk factor assessment and counseling
  - Provide general counseling regarding healthy lifestyle and activity promotion at every visit
  - Assess BP, BMI, waist circumference, dietary counseling, smoking cessation, lipid profile per guidelines

Primary Provider Role

- Reproductive counseling
  - Risk level 1,2- routine age appropriate counseling
  - Patients with aneurysms
    - Avoid contraception with risk of thrombosis
    - Multi-disciplinary team for pregnancy
    - Change in thromboprophylaxis therapy during pregnancy
Long term management

- **Activity Restrictions?**
  - Risk level 1-3 – no restrictions
  - Risk level 4-5
  - Self restriction
  - **High intensity activity or competitive sports guided by cardiac testing**
  - **No contact sports if on dual antiplatelet therapy / anticoagulation**

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**Medications**

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Low-Dose ASA</th>
<th>Anticoagulation (Warfarin or LMWH)</th>
<th>Dual-Antiplatelet Therapy (ASA+Clopidogrel)</th>
<th>β-Blocker</th>
<th>Statin</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. No treatment</td>
<td>Not indicated</td>
<td>Not indicated</td>
<td>Not indicated</td>
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<td>Not indicated</td>
</tr>
<tr>
<td>2. Illness only</td>
<td>Not indicated</td>
<td>Not indicated</td>
<td>Not indicated</td>
<td>Not indicated</td>
<td>Not indicated</td>
</tr>
<tr>
<td>3.1: Small aneurysm, current or persistent</td>
<td>Continue</td>
<td>May be considered</td>
<td>May be considered as an alternative to anticoagulation</td>
<td>Not indicated</td>
<td>Empirical therapy may be considered</td>
</tr>
<tr>
<td>3.2: Small aneurysm, regressed to normal or dilated only</td>
<td>Continue, but discontinuation may also be considered</td>
<td>Not indicated</td>
<td>Not indicated</td>
<td>Not indicated</td>
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<tr>
<td>5.1: Large and giant aneurysm, current or persistent</td>
<td>Continue</td>
<td>Reasonably indicated</td>
<td>May be considered in addition to anticoagulation</td>
<td>May be considered</td>
<td>Empirical therapy may be considered</td>
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<tr>
<td>5.2: Large or giant aneurysm, regressed to medium aneurysm</td>
<td>Continue</td>
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Summary

- KD is the leading cause of acquired heart disease in developed nations
- Significant mortality and morbidity if not recognized and treated early
- Long term surveillance and management of coronary stenosis and ischemia is critical
- Cardiovascular risk assessment and lifestyle counseling is integral to the management