Aortic Dilation and Dissection in Turner Syndrome: Update on Guidelines and New Evidence

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February 15, 2018
Turner syndrome (TS)

- 1:2500 females
- 50% 45,X
- 50% X chromosome derivatives
- Short stature
- Ovarian failure
- Skeletal abnormalities
**BAV and Coarctation are Common in TS**

- BAV rate in TS is 50 times its rate in the general population
- Dissection rates (NIH):
  - Population (8/100,000)
  - All TS (620/100,000)
  - TS+BAV (1,666/100,000)

30-40% 15-20% 25-30%
Larger Aortic Size Indices in TS Subjects with BAV

\[ P = 5 \times 10^{-7} \]
45,X Karyotype is Associated with BAV

Predictors: 45,X, neck webbing, chest wall deformity
Both Xp and Xq gene(s) contribute to CHD in TS

<table>
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<th></th>
<th>BAV</th>
<th>TAV</th>
<th>Total</th>
<th>%BAV</th>
<th>Copies of Xq</th>
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<tr>
<td>1 Non-mosaic</td>
<td>149</td>
<td>136</td>
<td>285</td>
<td>52</td>
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<tr>
<td>2 Mosaic non-iso</td>
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<td>28</td>
<td>1-2</td>
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<tr>
<td>3 Mosaic iso</td>
<td>18</td>
<td>41</td>
<td>59</td>
<td>30</td>
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<td>4 Non-mosaic iso</td>
<td>0</td>
<td>13</td>
<td>13</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>

Collapse 2 and 3: Chi-square (df=2) 27.39, P=0.000001
Risk Factors for Aortic Dissection in TS

- Hypertension
- Coarctation and/or Arch Elongation
- Aortic Dilation $Z > 3$
- Bicuspid Aortic Valve
Importance of Identifying Cardiovascular Abnormalities in TS

• Approximately 50% of all deaths in TS are due to CV disease

• Cause-specific mortality is significantly higher for aortic aneurysm and aortic valve disease

• Cumulative risk for death from aortic dissection is 200-fold higher than the general population

• Early diagnosis with appropriate management and monitoring may lead to improved long-term outcomes
Z-scores Identify At-Risk Patients Better than Absolute Aortic Diameters

Z-score calculators are available online: http://www.marfan.org/dx/zscore#formtop
Class I Adults

- TTE and CMR should be performed at the time of diagnosis.
- TTE or CMR surveillance studies should be performed at least every 10 years or prior to pregnancy.
- Systemic hypertension is a major risk factor for dissection and should be managed the same as for patients without TS.
- An increase in Z-score of 1 or an increase in aortic diameter of >0.5 cm over one year should prompt referral to a surgeon.

_Eur J Endocrinol_ 2017 Sep;177:G1-G70.
2016 International Consensus Guidelines
Class I Adults

Suggested Monitoring Protocol

> 16 years: Cardiology Exam, TTE, MRI, ECG

No CoA or BAV

Z<3

Low Risk

Repeat TTE or CMR every 10 years by primary managing clinician

Z>3

Moderate Risk

Repeat TTE or CMR every 3 – 5 years by primary managing clinician

CoA and/or BAV

Z<3

Moderate Risk

Repeat TTE or CMR every 3 – 5 years by primary managing clinician ± cardiologist

Z>3

High Risk

Repeat CMR every 1 – 2 years by cardiologist
2018 AHA Scientific Statement: Recommendations

- Diagnosis of bicuspid aortic valve or a left-sided obstructive lesion in a female should prompt genetic evaluation for TS

- Beta blockers and ACE inhibitors are recommended as first-line therapies

- Guidelines for surveillance and clinical management of cardiovascular disease should be applied equally to all TS patients regardless of karyotype.
TS Patients in your practice: What can you do?

- Refer to a TS Specialty Clinic:
  
  http://www.turnersyndrome.org/provider-directory
  http://tsgalliance.org/connect-to-ts-clinics/

- Participate in research:

  National Turner syndrome patient registry:  
  www.turnersyndrome.org/ts-registry-love

  Clinical research studies at UTHealth (NCT03185702)
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Acknowledgements

Cindy Scurlock
Michael Silberbach, MD

Tony Estrera, MD
Hazim Safi, MD
Dianna Milewicz, MD, PhD