Aortopathy in Pregnant Women with Turner Syndrome

Sorel Goland, MD

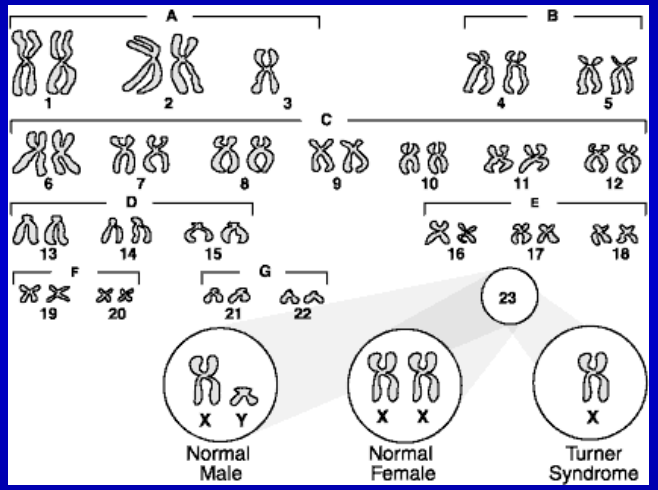
Associated Professor of Medicine

The Heart Institute, Kaplan Medical Center, affiliated to the Hebrew University, Jerusalem, Israel

The 4th International Congress on Cardiac Problems in Pregnancy (CPP2016)

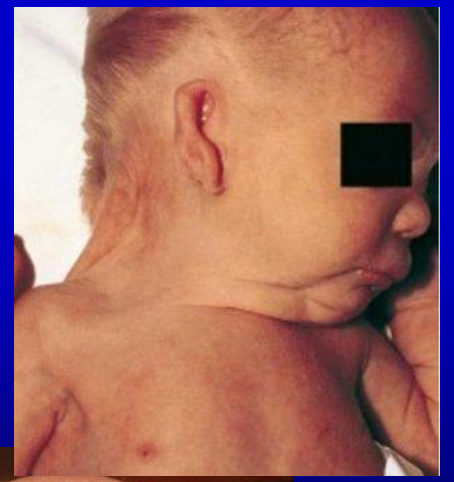
Turner syndrome

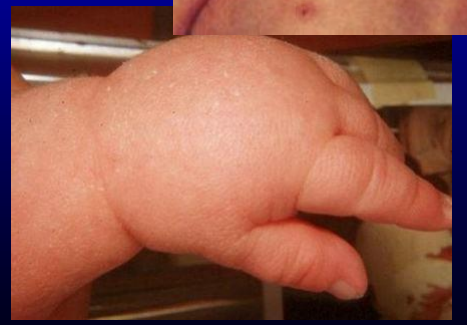
- One of the most common chromosomal disorders
- The most common genetic disorder in women
  - Loss of one X chromosome (45X0 vs. normal 46XX)
  - Deletion of the p arm of the X chromosome.
- May present as mosaic (45X0-46XX)
- Occurs ~ 1/2000 live-female birth



Main clinical features

- Short stature (143-145cm tall)
- Dysmorphic features (webbed neck, low-set ears, low hairline at the back)
- Lymphedema of hands and feet
- Early ovarian dysfunction





Pregnancy in women with TS

- Spontaneous pregnancy is rare ~7%

  (majority in mosaic for 45,X/46,XY)
- The oocyte donation is currently commonly used
- Implantation rates are equal to non-TS
- The miscarriage rate is higher than normal ~40%.
- A tendency for C-section in most cases due to small maternal size

Karnis MF et al, Fertility and Sterility 2003;80:498– 501.
Birkebaek NH et al, G. Clinical Genetics 2002;61:35–39
Mosquera M & De Backer J. Expert Review of Cardiovasc Therapy, 2015; 13:6, 703-714

Congenital cardiovascular defects

~50% of young women with TS

- Bicuspid aortic valve (BAV) ~20%
- Aortic coarctation (CoA) ~ 10%
- Partial anomalous pulmonary connection ~ 18%
- Anomalous origin of the right subclavian ~8%
- Clinically severe defects 10–15%
- Are more prone to develop hypertension

Mortensen KH, Andersen NH, Gravholt CH.Endocr Rev 677-714:(5)33;2012

The most serious medical problem : an increased risk for aortic dissection

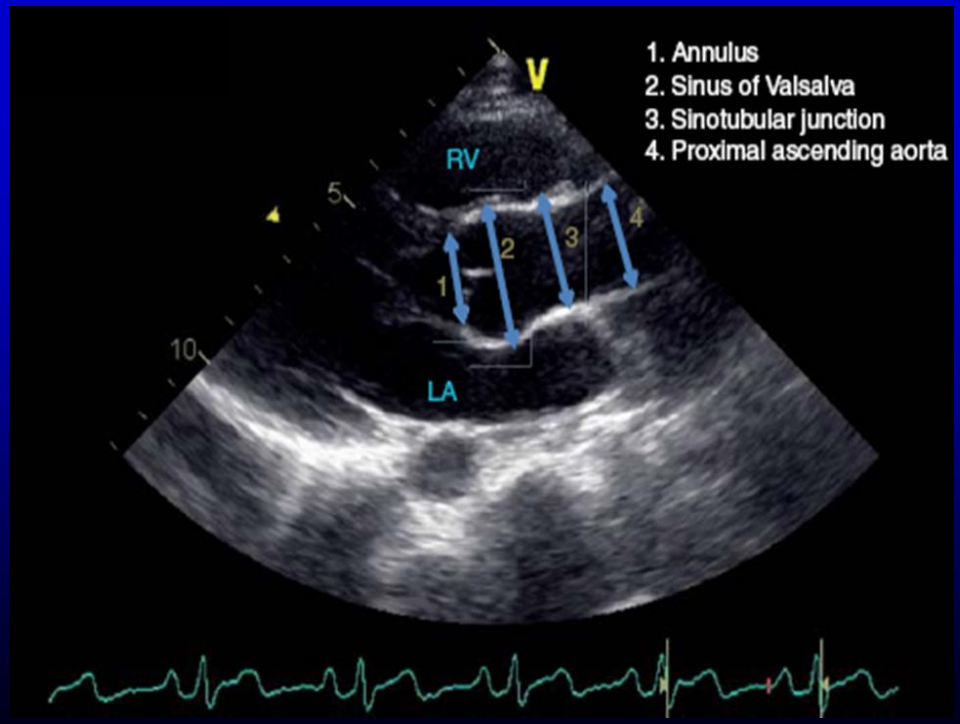
Risk factors for aortic dissection

- aortic dilatation
- bicuspid aortic valves
- coarctation of the aorta
- pregnancy

The assessment of aortic dilatation in TS

- Although the ascending aortic diameter is normal in absolute numbers, the smaller stature means that these patients in fact have dilated aortas

Aortic size index (aortic diameter /body surface area) (ASI)



Aortic dissection (AoD) in TS in pregnancy

- The incidence of an AoD is 6 times higher than in general young population
- ~10% of AoD are related to pregnancy
- Higher rate of aneurysm formation and progression during pregnancy
- The risk of maternal death from AoD during pregnancy is higher than in women in general population
- The maternal risk of death is not well demarcated , but has been estimated to be ~ 2.0%

Carlson M, Silberbach M. J Med Genet 2007;44:745-9.Bondy CA. Curr Opin Cardiol 2008;23:519-26.
The Practice Committee of the American Society for Reproductive M. Fertility and Sterility 2005;83:1074–1075.
Karnis *MF. Fertil Steril. 2012 ;98(4)*:787-91

Aortic dissection in TS in pregnancy

The International Turner syndrome Aortic dissection Registry

- 20 young women
- 1 case out of 19 (5%) was associated with pregnancy
- 3 patients had a history of pregnancy before AoD
- 1 case of uneventful pregnancy 2 years after AoD
- Smaller aortic diameters than in the general population (ASI>2.5 cm/m^2)
- Cardiac malformations, including BAV

Carlson M, Airhart N, Lopez L, Silberbach M.Circulation 2012;126:2220-6.

Aortic dissection in 158 women with TS

- 3 cases of aortic dissections (3 years follow-up)= an incidence of ≈618 cases per 100 000 TS-years
- All women with ASI of >2.5 cm/m²

Prophylactic aortic surgery should be recommended in any individual with TS >18 y.o including those contemplating pregnancy with an ASI>2.5 cm/m²

Matura LA, Ho VB, Rosing DR, Bondy CA. Circulation 2007;116:1663-70.

Aortic dissection in TS in pregnancy

122 cases

- 14 cases of pregnancy-associated AoD with mortality rate of 77%
- 5 women with BAV and 3 with coarctation of the aorta
- Most patients had aortic size index (ASI) >2.5 cm/m².
- 7 had AoD during the 3rd trimester and 3 patients postpartum (at 1-2 weeks).

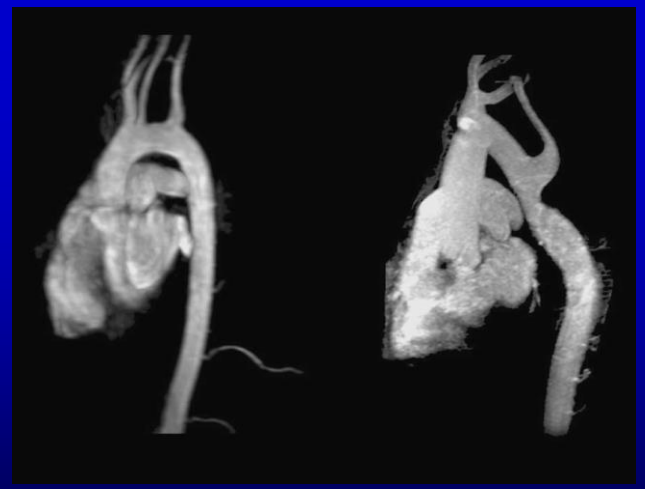
ASI>2.5 cm/m², or those with an ASI>2.0 cm/m² + BAV and/or CoA and uncontrolled HTN should be advised against pregnancy

Wong SC, Cheung M, Zacharin M. Int J Adolesc Med Health 2014;26:469-88.

Preconception pregnancy counseling

Careful assessment of cardiovascular involvement is mandatory

- only ~50% of TS patients had a screening echocardiogram prior to fertility treatment
- in ~30% of cases adequate visualization of the aortic valve and aorta were impossible



Adapted from Ho et al. Circulation 2004;110:1694–1700.

Preconception pregnancy counseling

- Special attention should be paid to the aortic dimensions assessment (ASI) using echo (TTE, TEE), and when needed CT or MRI.

- ESC on management of CVD in pregnancy suggest prophylactic surgery in women with TS with an ASI>2.7 cm/m²
- But recent reports and guidelines strongly recommend surgery in those with ASI>2.5 cm/m²

ESC Guidelines on the management of cardiovascular diseases during pregnancy. Eur Heart J 2011;32:3147-97.
Matura LA, Ho VB, Rosing DR, Bondy CA. Circulation 2007;116:1663-70
Boodhwani M, Andelfinger G, Leipsic J, et al. Can J Cardiol 2014; 30(6):577-89

Specific recommendations during pregnancy for women with TS aortopathy

- Treatment of hypertension
- Echo and cardiology consult every 4-6 weeks
- Women with aortic size index < 2.5 cm/m² -vaginal delivery
- *Aortic growth of ≥10% or ASI ≥ 2.5 cm/m² or > 2.0 cm/m² with other risk factors* require admission and close monitoring with delivery by cesarean section

The Practice Committee of the American Society for Reproductive M. Fertility and Sterility 2005;83:1074–1075.
Mosquera M & De Backer J. Expert Review of Cardiovascul Therapy, 2015; 13:6, 703-714

Specific recommendations during pregnancy for women with TS

- If AoD occurs during pregnancy, surgery is indicated
  - before 25 weeks with the fetus in utero
  - above 25 weeks cesarean section followed by surgery
- Beta-blocker therapy can be considered
- Women with Turner syndrome even with a normal echocardiogram require careful observation & reevaluation throughout gestation.

The Practice Committee of the American Society for Reproductive M. Fertility and Sterility 2005;83:1074–1075.
Mosquera M & De Backer J. Expert Review of Cardiovascul Therapy, 2015; 13:6, 703-714

Thank you!