Fertility treatment in women with heart disease

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No conflicts of interest.
Cardiovascular disease

In 1-4% of all pregnancies
Incidence is rising
• Increasing age at first pregnancy
• Increasing prevalence risk factors: obesity
• Women with cong. CVD reach childbearing age
• Immigrants with undiagnosed conditions
Changes in pregnancy

- Cardiac output
- Blood volume
- Heart rate
- Stroke volume

Per cent change

First trimester  Second trimester  Third trimester  Postpartum 6 months
Maternal mortality

Fewer women are dying from emergency pregnancy complications

1987-'90

28.7%
19.7
17.6
2.5

2006-'10

14.9% pregnancy-induced hypertension
11.4% hemorrhage
4.8
0.7 anesthesia complications

Percentage of pregnancy-related deaths due to a specific complication

World 200/ 100.000
EU + USA 20/ 100.000
Africa 400/ 100.000
Maternal mortality

Fewer women are dying from emergency pregnancy complications

1987-'90

28.7%

1987-'90

2006-'10

20610

11.4% hemorrhage

5.6

14.9

13.1

4.8

0.7 anesthesia complications

Pregnancy-induced hypertension

The percentage of pregnancy deaths caused by chronic diseases is steadily rising

2006-'10

14.6%

cardiovascular conditions

3%

11.8

cardiomyopathy

5.6

13.6

infections

SOURCE: CDC Pregnancy Mortality Surveillance System
CREDIT: Sarah Frostenson
Maternal mortality

Fewer women are dying from emergency pregnancy complications

1987-’90

Percentage of pregnancy-related deaths due to a specific cause

28.7%

19.7

17.6

2.5

24.3% cardiac

4.8 pregnancy-induced hypertension

0.7 anesthesia complications

World: 200/100,000
EU and USA: 20/100,000
Africa: 400/100,000

The percentage of pregnancy deaths caused by cardiovascular diseases is steadily rising
2006-’10

14.6% cardiovascular conditions
11.8 cardiomyopathy
13.6 infections
5.6

EU and USA: congenital heart defects
Africa: rheumatic valvular disease

SOURCE: CDC Pregnancy Mortality Surveillance System
CREDIT: Sarah Frostenson
## Modified WHO risk classification

<table>
<thead>
<tr>
<th>Risk class</th>
<th>Risk of maternal mortality</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>No increased risk</td>
<td>Mild pulmonary stenosis Mitral prolapse</td>
</tr>
<tr>
<td>II</td>
<td>Small increased risk</td>
<td>Unoperated ASD or VSD Repaired tetralogy of Fallot</td>
</tr>
<tr>
<td>III</td>
<td>Significantly increased risk</td>
<td>Mechanical valve Hypertrophic cardiomyopathy Fontan circulation Aortic dilatation in Marfan</td>
</tr>
<tr>
<td>IV</td>
<td>Extreme high risk; pregnancy contraindicated</td>
<td>Pulmonary arterial hypertension Severe mitral or aortic stenosis Severe coarctation</td>
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ESC Guidelines, Eur Heart J 2011
CVD and infertility

- Risk of miscarriage and poor fetal outcome
- Co-incidental infertility
- Requests for ART (PGD, oocyte donation, surrogacy)

Drenthen et al, JACC 2007
Fertility treatment?

Shared decision *and* responsibility team

1. Risks of fertility treatment acceptable?
2. Risks of pregnancy acceptable?
3. Interest of future child?

   Health and life expectancy of mother

Transmission of CVD 3-50%
IVF

- Clotting factors increase after hCG (not E2)
- Ovum pick-up and anticoagulation
- OHSS: hypovolemia, hypotension, VTE, ATE
- Multiple pregnancies to be prevented
- Donor oocytes: risk of pre-eclampsia 20-40%
Aortic disease

• Predispose to aneurysm and dissection
• Leading cause of maternal mortality
• Heritable disorders of connective tissue: Marfan, Ehlers-Danlos, Turner
Turner syndrome

- Short stature
- Low hairline
- Shield-shaped thorax
- Widely spaced nipples
- Shortened metacarpal IV
- Small finger nails
- Brown spots (nevi)
- Characteristic facial features
- Fold of skin
- Constriction of aorta
- Poor breast development
- Elbow deformity
- Rudimentary ovaries
- Gonadal streak (underdeveloped gonadal structures)
- No menstruation
Turner syndrome

- Short stature
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Characteristic facial features:
- Fold of skin
- Constriction of aorta
- Poor breast development
- Elbow deformity

- Rudimentary ovaries
- Gonadal streak (underdeveloped gonadal structures)

- No menstruation

- < 20% spont menarche
- < 5% spont pregnancies
Turner syndrome

- Short stature
- Low hairline
- Shield-shaped thorax
- Widely spaced nipples
- Shortened metacarpal IV
- Small finger nails
- Brown spots (nevi)
- Characteristic facial features
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- Construction of aorta
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- No menstruation

Additional information:

- 25% hypertension
- 20% bicuspid aortic valve
- 10% coarctation aorta
Turner syndrome

- Short stature
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Inheritable disorder of connective tissue

- 25% hypertension
- 20% bicuspid aortic valve
- 10% coarctation aorta

Predisposes to aneurysm and dissection
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Characteristics:
- Fold of skin
- Constriction of aorta
- Poor breast development
- Thumb deformity
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Inheritable disorder of connective tissue

- 25% hypertension
- 20% bicuspid aortic valve
- 10% coarctation aorta

Predisposes to aneurysm and dissection

Donor oocytes
Pre-eclampsia
Risk of death in pregnancy achieved through oocyte donation in patients with Turner syndrome: a national survey

Megan Freebury Karnis, M.D., Alison Elizabeth Zimon, M.D., Sasmita Indra Lalwani, M.D., Lorna Smink Timmreck, M.D., Sigal K lipstein, M.D., and Richard Henry Reindollar, M.D.

Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Reproductive Biology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, IVF, Boston, Massachusetts

... risk of death from rupture or dissection of the aorta in pregnancy may be 2% or higher. Patients with TS have not been adequately screened before treatment...
ASRM guidelines 2012

In all TS patients contemplating pregnancy:

- Evaluation for hypertension, aortic size, bicuspid aortic valve, coarctation
- MRI for aortic size index (corrected for body surface area)
ASRM guidelines 2012

- TS is relative contraindication for pregnancy
- Hypertension, bicuspid aortic valve, coarctation and/or ASI >2 cm/m2 is absolute contraindication for pregnancy
- TS women with normal evaluation are still at high risk for aortic dissection
Obstetric and neonatal outcome after oocyte donation in 106 women with Turner syndrome: a Nordic cohort study

Anna Hagman¹,*, Arne Loft², Ulla-Britt Wennerholm¹, Anja Pinborg², Christina Bergh³, Kristiina Aittomäki⁴, Karl-Gösta Nygren⁵, Liv Bente Romundstad⁶,⁷, Johan Hazekamp⁸, and Viveca Söderström-Anttila⁹

Pregnancies between 1992-2011
## Pregnancy outcome

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<td>Life threatening complications</td>
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* No screening before 2000
Spontaneous fertility and pregnancy outcomes amongst 480 women with Turner syndrome

Valérie Bernard¹,², Bruno Donadille¹,², Delphine Zenaty³,⁴,⁵, Carine Courtillot⁶, Sylvie Salenave⁷, Aude Brac de la Perrière⁸, Frédérique Albare⁹,¹⁰, Anne Fèvre¹¹, Véronique Kerlan¹², Thierry Brue⁹,¹⁰, Brigitte Delemer¹¹, Françoise Borson-Chazot⁸, Jean-Claude Carel³,⁴,⁵, Philippe Chanson⁷, Juliane Léger³,⁴,⁵, Philippe Touraine⁶, and Sophie Christin-Maitre¹,²,* for CMERC Center for Rare Disease

Pregnancies between 1999-2014
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Fertility treatment in women with heart disease

- Conclusions -

• CVD is leading cause of overall maternal mortality
• Balance risks and benefits (for mother and child) in multidisciplinary team with cardiologist and obstetrician
• Pre-pregnancy evaluation in TS is mandatory, but risk of aortic dissection cannot be excluded
• Refrain from fertility treatment if there is a high risk of serious harm