BSH Heart Failure Day for Revalidation and Training 2017

What to do when a heart failure patient becomes pregnant

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Conflicts of interest - sponsorship, consultancy and speaker fees:
Medtronic, St Jude, Boehinger, Astra Zeneca
Structure

- Introduction
  - Planning pregnancy - known HF patient
  - Your HF patient becomes pregnant
  - New HF during pregnancy
  - Multidisciplinary approach
Figure 1: Summary of Physiological Changes Occurring During Pregnancy

- Plasma volume by 40%
- Physiological anaemia
- Cardiac output by 30–50%
- Cardiac output during delivery/postpartum
- Systematic vascular resistance
- Transient LV dilatation
- Hypercoagulable state
- Weeks to months for CO and SVR to normalise

CO = cardiac output; LV = left ventricle; SVR = systemic vascular resistance.
Physiology of pregnancy

High-Risk Cardiac Disease in Pregnancy
Part I

Uri Elkayam, MD; Sorel Goland, MD; Petronella G. Peeper, MD; Candice K. Silversides, MD

JACC 2016;68:396-410

Percent changes in heart rate, stroke volume, and cardiac output measured in the lateral position throughout pregnancy compared with pre-pregnancy values. Adapted from Elkayam and Gleicher (1) and Robson et al. (103).
More than 50 years of confidential enquiries
Causes of maternal death

189 cardiac deaths
UK & Ireland 2009-2014

Cardiac disease is the leading cause of indirect maternal death and the leading overall cause of maternal mortality
Maternal deaths from cardiac causes

Actual number of maternal deaths from cardiac causes

- 1985-1987
- 1988-1990
- 1991-1993
- 1994-1996
- 1997-1999
- 2000-2002
- 2003-2005
- 2006-2008
- 2009-2011
- 2011-2014
Type of cardiac disease causing death

- Congenital
- Acquired (IHD)
- Acquired (Other Causes)
Maternal mortality increases with age
Cardiac deaths from MBRRACE 2009-2014.

- Hypertensive heart disease
- Peripartum cardiomyopathy
- Valvular heart disease
- Congenital heart disease
- Aortic dissection
- Cardiomyopathy/myocardial disease
- Ischaemic heart disease
- SADS (morphologically normal)

Actual numbers represented.

11 congenital deaths and 9 PPCM deaths are included in other figures and are shown for illustration only.
ESC Guidelines on the management of cardiovascular diseases during pregnancy

The Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC)

Management of Pregnancy in Patients With Complex Congenital Heart Disease

A Scientific Statement for Healthcare Professionals From the American Heart Association

Circulation. 2017;135:00-00
Structure

- Introduction
- Planning pregnancy - known HF patient
- Your HF patient becomes pregnant
- New HF during pregnancy
- Multidisciplinary approach
Preconception counselling

- Planning vital
- Time to assess LV function and cardiac reserve
- Time to stop ACE inhibitors
- Time to assess if there will be deterioration off ACE inhibitors
- Woman and partner need to be aware of potential risks of pregnancy (mortality)
- Risk of pregnancy leading to further decline in functional status that may not return to baseline
## Table 7  Modified WHO classification of maternal cardiovascular risk: application

<table>
<thead>
<tr>
<th>Conditions in which pregnancy risk is WHO I</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Uncomplicated, small or mild</td>
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<tr>
<td>- pulmonary stenosis</td>
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<tr>
<td>- patent ductus arteriosus</td>
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<tr>
<td>- mitral valve prolapse</td>
</tr>
<tr>
<td>• Successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, anomalous pulmonary venous drainage).</td>
</tr>
<tr>
<td>• Atrial or ventricular ectopic beats, isolated</td>
</tr>
</tbody>
</table>

### Conditions in which pregnancy risk is WHO II or III

**WHO II (if otherwise well and uncomplicated)**

- Unoperated atrial or ventricular septal defect
- Repaired tetralogy of Fallot
- Most arrhythmias

**WHO II/III (depending on individual)**

- Mild left ventricular impairment
- Hypertrophic cardiomyopathy
- Native or tissue valvular heart disease not considered WHO I or IV
- Marfan syndrome without aortic dilatation
- Aorta <45 mm in aortic disease associated with bicuspid aortic valve
- Repaired coarctation

**WHO III**

- Mechanical valve
- Systemic right ventricle
- Fontan circulation
- Cyanotic heart disease (unrepaired)
- Other complex congenital heart disease
- Aortic dilatation 40–45 mm in Marfan syndrome
- Aortic dilatation 45–50 mm in aortic disease associated with bicuspid aortic valve

**Conditions in which pregnancy risk is WHO IV (pregnancy contraindicated)**

- Pulmonary arterial hypertension of any cause
- Severe systemic ventricular dysfunction (LVEF <30%, NYHA III–IV)
- Previous peripartum cardiomyopathy with any residual impairment of left ventricular function
- Severe mitral stenosis, severe symptomatic aortic stenosis
- Marfan syndrome with aorta dilated >45 mm
- Aortic dilatation >50 mm in aortic disease associated with bicuspid aortic valve
- Native severe coarctation

Adapted from Thorne et al. LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; WHO = World Health Organization.
## Risk scoring systems

**Table 3**

<table>
<thead>
<tr>
<th>Predictors from CARPREG study</th>
<th>Predictors from ZAHARA studies</th>
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</thead>
<tbody>
<tr>
<td>Systemic ventricular impairment (EF &lt;40%)</td>
<td>History of arrhythmic event</td>
</tr>
<tr>
<td>Prior cardiovascular event</td>
<td>Baseline functional NYHA Class &gt; II</td>
</tr>
<tr>
<td>New York Heart Association (NYHA) Class ≥ II</td>
<td>Left heart obstruction (peak gradient &gt;50 mm Hg)</td>
</tr>
<tr>
<td>Cyanosis (SaO&lt;sub&gt;2&lt;/sub&gt; &lt;90%)</td>
<td>Mechanical valve prosthesis</td>
</tr>
<tr>
<td>Severe left heart obstruction</td>
<td>Moderate/severe atroventricular valve regurgitation (due to associated ventricular dysfunction)</td>
</tr>
<tr>
<td></td>
<td>Unrepaired cyanotic heart disease</td>
</tr>
<tr>
<td></td>
<td>Use of cardiac medication prior to pregnancy</td>
</tr>
</tbody>
</table>

Adapted from Siu et al. [4].

Score derived by assigning a point to the presence of each feature. Risk of maternal adverse event according to score: 0 = 5%, 1 = 27%, >1 = 75%.
Maternal functional capacity

- Maternal functional capacity predicts ability to tolerate pregnancy
- Many patients under report or under recognise degree of limitation
- Objective assessment of functional capacity
- Cardiopulmonary exercise test or exercise stress test
Grewal et al JACC 2010

- 36 pregnancies in 32 women
  - 27 idiopathic DCM
  - 5 doxorubicin induced cardiomyopathy
- 50% mild LVSD
- 22% moderate LVSD
- 28% severe LVSD
- 67% NYHA I
- 17% NYHA II
- 17% NYHA III-IV

All women with adverse cardiac events during pregnancy had moderate or severe LVSD, NYHA III/IV or previous adverse event
Adverse events/maternal risk factors
Pregnancy – negative impact on clinical course of DCM

Appropriate contraception

- Vital for women counselled against pregnancy or women who choose not to pursue pregnancy
- Combined oestrogen-progesterone pill
- Progesterone only contraception:
  - Depot injection
  - Subcutaneous implant
  - Progesterone only pill
- Intrauterine device eg Mirena coil
- Sterilisation
Introduction
Planning pregnancy - known HF patient
Your HF patient becomes pregnant
New HF during pregnancy
Multidisciplinary approach
Registry on Pregnancy and Cardiac Disease (ROPAC)

- 1321 pregnancies, 28 countries
- 86% developed countries – 74% congenital
- Developing countries – 72% valvular heart disease

\[ n = 1321 \text{ patients} \]

Heart failure: 13% (n=173)

Deaths: 13/1321 (0.1%)

Ruys et al, Heart 2014;100:231-238
Predictors of HF in pregnancy

- Signs of HF prior to pregnancy
- NYHA class III or IV
- Structural heart disease: WHO category >3
- Cardiomyopathy
- Pulmonary hypertension
- Preeclampsia during pregnancy OR 7.1
- Registry of structural heart disease – 30% with preeclampsia also developed HF
Medical Treatment of Heart Failure in peripartum women

Non Pregnant (cardiomyopathy): According to standard heart failure guidelines

Early Pregnancy: Diuretics, Hydralazine, Beta Blocker

Late Pregnancy: Diuretics, Hydralazine, Beta Blocker

Postpartum: Diuretics, Ace-inhibitor, Beta blocker
ACEi/ARB during pregnancy

Bullo M et al, Hypertension 2010;60:444-450
Pregnancy Outcome Following Exposure to Angiotensin-Converting Enzyme Inhibitors or Angiotensin Antagonists: A Systematic Review
Birthweight and beta blockers

Cardiac medication during pregnancy, data from the ROPAC

Titia P.E. Ruys, Aldo Maggioni, Mark R. Johnson, Karen Sliwa, Luigi Tavazzi, Markus Schwerzmann, Petros Nihoyannopoulos, Mirta Kozelj, Ariane Marelli, Uri Elkayam, Roger Hall, Jolien W. Roos-Hesselink
Labour

- Contractions cause pain and anxiety which increases cardiac output
- Uterine contractions push 400mls blood into the circulation – increased CVP and arterial pressure
- Pelvic descent of fetus causes urge to bear down
- Valsalva manoeuvre – avoid in aortic stenosis, Marfan/aortopathy or pulmonary HT
Cardiac output during labour

Managing labour

- Aim 37 weeks or more
- Early epidural analgesia
- Facilitated second stage of labour
- Consider corticosteroids for fetal lung immaturity
- Induction of labour can precipitate tachycardias and decreased SVR
- O₂ sats monitoring
- Sometimes arterial line
- Care with IV fluids – meticulous management of blood loss during delivery
Postpartum

- 500mls of blood from contracted uterus
- Increased preload via vena caval decompression
- Cardiac output increases rapidly by 60-80%
- Dissipates within an hour
- Also blood loss from delivery
  - 600mls for vaginal delivery
  - 1000mls from caesarean section
After delivery

- Reassess volume status
- Frequent clinical evaluations
- High risk period for first 48 hrs to two weeks postpartum
- Restart ACE inhibitors: enalapril and captopril fine with breastfeeding
- Beta blockers fine with breastfeeding (avoid atenolol)
Structure

- Introduction
- Planning pregnancy - known HF patient
- Your HF patient becomes pregnant
- **New HF during pregnancy**
- Multidisciplinary approach
77% of cardiac deaths in pregnancy occur in patients not known to have heart disease.
BNP in pregnancy

- BNP >100 pg/ml were found in 10% of women with heart disease by the first trimester and in 26% of women by the third trimester.
- None of the healthy control subjects had a BNP >100 pg/ml at any time.

Causes of heart failure in pregnancy

- Familial cardiomyopathy
- Rheumatic heart disease
- Congenital heart disease
- Prosthetic valve – is the valve clotting?
- Peripartum cardiomyopathy
- ACS/coronary dissection
- Pulmonary hypertension
- Pulmonary embolism – right heart failure
Timing of heart failure in pregnancy

4.8% mortality

Ruys et al, Heart 2014;100:231-238
Peripartum cardiomyopathy

- Idiopathic cardiomyopathy
- Presents with heart failure secondary to LV systolic dysfunction
- Towards the end of pregnancy or in the months following delivery
- Diagnosis of exclusion when no other cause of heart failure is found
- LV may not be dilated, but the EF is nearly always reduced below 45%

- Occurs in around 1~2000 births
Current management of patients with severe acute peripartum cardiomyopathy: practical guidance from the Heart Failure Association of the European Society of Cardiology Study Group on peripartum cardiomyopathy

Johann Bauersachs¹, Mattia Arrigo²,³, Denise Hilfiker-Kleiner¹, Christian Veltmann¹, Andrew J.S. Coats⁴, Maria G. Crespo-Leiro⁵, Rudolf A. De Boer⁶, Peter van der Meer⁶, Christoph Maack⁷, Frederic Mouquet⁸, Mark C. Petrie⁹, Massimo F. Piepoli¹⁰, Vera Regitz-Zagrosek¹¹, Maria Schaufelberger¹², Petar Seferovic¹³, Luigi Tavazzi¹⁴, Frank Ruschitzka³, Alexandre Mebazaa¹⁵, and Karen Sliwa¹⁶
Assess Cardiopulmonary Distress

- SBP < 90 mmHg
- HR > 130/min or < 45/min
- RR > 25/min
- SpO2 < 90%
- Lactate > 2.0 mmol/L
- Altered mental state
- Cold skin
- Oliguria

Confirm Diagnosis

- ECG
- CXR
- Blood tests
- BNP
- Echo
- Lung ultrasound
- Exclude differential diagnoses
Acute HF during pregnancy

- Multidisciplinary team within 15 minutes
  - Cardiologist, obstetrician, neonatologist, anaesthetist, surgeon
- Status and prognosis of fetus
  - If non-viable: urgent delivery
  - Maximal HF therapy
- If viable need to consider urgent delivery versus continuing pregnancy
  - Corticosteroids for fetal lung maturation
Severe HF with cardiopulmonary distress

- Optimise preload
  - Diuretics/vasodilators/volume
- Optimise oxygenation
  - CPAP/NIV/invasive ventilation
- Add inotropes and/or vasopressors
- Urgent delivery (caesarean section)
- Consider bromocriptine 2.5mg bd
- Consider mechanical circulatory support
PPCM without cardiopulmonary distress

**Antepartum**
- HF therapy
  - Hydralazine
  - Nitrates
  - BB (metoprolol)
  - Consider diuretics
- Consider delivery
  (vaginal delivery with PDA)

**Postpartum**
- HF therapy
  - ACEi (or ARB)
  - BB
  - Spironolactone
  - Diuretics
  - Consider ivabradine
- Consider bromocriptine
  (2.5 mg bid)

**Consider WCD therapy**
if LVEF ≤ 35%

**Continue HF therapy**
for ≥ 12 months after recovery of LV-function
Anticoagulation

- Hypercoaguable state of pregnancy persists for 8 weeks postpartum

- LV thrombus common if EF < 35%
  - Smoke on echo
  - LV > 65mm
  - Previous emboli

- Anticoagulate with heparin
European Journal of Heart Failure (2014)
doi:10.1002/ejhf.68

ROPAC
Registry Of Pregnancy And Cardiac disease

EUROobservational Research Programme: a worldwide registry on peripartum cardiomyopathy (PPCM) in conjunction with the Heart Failure Association of the European Society of Cardiology Working Group on PPCM
Summary

- Dyspnoea might be normal in pregnancy but think HF
- Assess and treat – BNP useful, avoid ACEi/ARB
- Multidisciplinary approach
- Acute dramatic presentation needing circulatory support?
- Can we manage this here or should this lady be somewhere else?
- Pick up the phone – call people, get help
Cardiovascular changes of pregnancy

- Blood volume increases by 40% peaking at 32 weeks
- Oestrogen upregulates renin angiotensin system
- Plasma volume expansion is by sodium and water retention
- Falling oncotic pressure due to less albumin
- Uterine compression of the IVC leads to increased femoral venous pressure
- Higher risk of pulmonary oedema
Subsequent pregnancy

Hilfiker-Kleiner EHJ doi:10.1093/eurheartj/ehv009
**FIGURE 2** Maternal Complications Associated With Subsequent Pregnancy in 44 Patients With a History of Peripartum Cardiomyopathy

*Slate bars* are group 1, women with left ventricular ejection fraction (LVEF) ≤ 50% before subsequent pregnancy. *Salmon bars* are group 2, women with LVEF < 50% before subsequent pregnancy. HF = heart failure. Reprinted with permission from Elkayam et al. (10).
20 patients
Bromocriptine blocks prolactin
- 16 kDa Form of prolactin key
to developing PPCM
Bromocriptine

- Oxidative stress cleaves prolactin into harmful 16 kDa pathological form
- Influenced by inflammatory/autoimmune factors
- Block prolactin: improves outcome
- Bromocriptine blocks prolactin
- German Bromocriptine group – ethics committee did not allow ‘no bromocriptine’ arm – 7 days vs 6 weeks treatment
**VEGF:**
Vascular endothelial growth factor
Targets growth and health of small blood vessels (beneficial)

**sFLT1:**
anti-angiogenic molecule released by the placenta – causes HT of pre-eclampsia (harmful)

**Bromocriptine suppresses prolactin so it cannot be cleaved into anti-angiogenic 16kD form** (beneficial)

Prolactin cleaved into 16kD form is anti-angiogenic (harmful)
Long-term cardiomyopathy survival

Felker et al NEJM 2000;342:1077