• Dyspnoea and leg swelling, when is it heart failure?

• Management of acute decompensated heart failure

• Heart failure during pregnancy

• Refractory oedema in heart failure patient
Late maternal deaths: a neglected responsibility

Sliwa K, Anthony A. The Lancet 2016; 387: 2072-2073

Maternal mortality, no matter when and where it occurs, results in sequelae that extend beyond the loss of the life of a single woman.

Most countries record maternal death only up to 42 days postpartum because of the assumption that avoidable death in pregnant women occurs during pregnancy or shortly thereafter.

The International Classification of Diseases Code (ICD10) makes it obligatory to document the occurrence of pregnancy within a year of the death of any woman.

What is known is that late maternal deaths fall into the main categories: cardiovascular causes, thromboembolism, and suicide (likely linked to postpartum depression).

Globally, there are more postpartum and late maternal deaths from direct and indirect obstetric causes than maternal deaths during pregnancy.

Postpartum and late maternal deaths have not declined in the past decade, whereas deaths in the peripartum period have.
PPCM (34%) and complications of RHD (25.3%) were the most important causes of heart failure and maternal death.

**Fig. 3.** Cardiovascular conditions contributing to cardiac death ($n = 118$).

<table>
<thead>
<tr>
<th>Avoidable factors</th>
<th>Whole group</th>
<th>Peripartum cardiomyopathy</th>
<th>Rheumatic heart disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient delay in seeking help</td>
<td>49 (41.5)</td>
<td>16 (39.0)</td>
<td>16 (45.7)</td>
</tr>
<tr>
<td>Lack of expertise by medical staff managing case</td>
<td>35 (29.7)</td>
<td>16 (39.0)</td>
<td>12 (34.3)</td>
</tr>
<tr>
<td>Delay in referral to appropriate level of care</td>
<td>31 (26.3)</td>
<td>13 (31.7)</td>
<td>8 (22.9)</td>
</tr>
<tr>
<td>Delay in appropriate action</td>
<td>43 (36.4)</td>
<td>15 (36.6)</td>
<td>15 (42.9)</td>
</tr>
</tbody>
</table>
A 33 year old women presented to the admission ward at a secondary hospital with shortness of breath, pedal oedema

**History:** No family Hx of CVD, no previous cardiac disease, 3 children and now 2 month post delivery

**Clinical examination:** BP: 95/65 mmHg, HR 110 bpm, basal crackles, 2+ pedal oedema

**CXR:** enlarged cardiac silhouette and signs of pulmonary congestion.
CASE STUDY II

Heart failure during pregnancy

[ECG strips shown with labels for leads I, II, III, aVR, aVL, aVF, V1 to V6]
CASE STUDY II:
Heart failure during pregnancy

Cardiac ultrasound:
CASE STUDY III:

Heart failure during pregnancy

Cardiac MRI
A practical approach

Differential diagnosis

1. Patients can have a known pre-existing heart disease, such as congenital heart disease, Marfan’s, cardiomyopathy, rheumatic heart disease and valve prosthesis.

2. Patients can present with a newly diagnosed heart disease unmasked by pregnancy, familial cardiomyopathy, undiagnosed rheumatic heart disease, undiagnosed congenital heart disease.

3. Patients can have a newly developed heart disease, such as peripartum cardiomyopathy, acute coronary syndrome, gestational hypertension/preeclampsia/ severe hypertension, leading to heart failure.
Does geographic location matter?

**Higher income regions:** maternal age, obesity, hypertension, preexisting coronary artery disease, operated congenital heart disease

**Lower income regions:** rheumatic heart disease, Chagas cardiomyopathy, unoperated congenital heart disease

**All regions:** Increase in diagnosis of cancer induced cardiomyopathy, left ventricular non compaction cardiomyopathy, peripartum cardiomyopathy
How to risk stratify a high risk pregnancy woman
Modified WHO Classification of Maternal Cardiovascular Risk

### WHO II – maternal cardiac event rate: 5-10%
- Unoperated atrial or ventricular septal defect
- Repaired tetralogy of Fallot
- Most arrhythmias
- Mild left ventricular impairment
- Hypertrophic cardiomyopathy
- Native or tissue valvular heart disease
- Marfan syndrome without aortic dilatation; Aorta <45 mm in aortic disease associated with bicuspid valve
- Repaired coarctation

### WHO III – maternal cardiac event rate: 19-27%
- 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

---

Modified WHO Classification of Maternal Cardiovascular Risk

**Conditions in which pregnancy risk is WHO IV (pregnancy contraindicated)**
*maternal cardiac event rate: 40-100%*

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary arterial hypertension of any cause</td>
</tr>
<tr>
<td>Severe systemic ventricular dysfunction (LVEF &lt;30%, NYHA III-IV)</td>
</tr>
<tr>
<td>Previous peripartum cardiomyopathy with any residual impairment of left ventricular function</td>
</tr>
<tr>
<td>Severe mitral stenosis, severe symptomatic aortic stenosis,</td>
</tr>
<tr>
<td>Marfan syndrome with ascending aorta &gt; 45 mm</td>
</tr>
<tr>
<td>Bicuspid aortic valve with ascending aortic diameter &gt;50 mm</td>
</tr>
<tr>
<td>Native severe coarctation</td>
</tr>
</tbody>
</table>

LVEF = left ventricular ejection fraction;
NHYA = New York Heart Association;
WHO = World Health Organization

Preconception Evaluation

All women with heart disease should ideally have preconception evaluation, including advice on risk prediction and contraception by a joint cardiac-obstetric team seeking advice from other specialities.

<table>
<thead>
<tr>
<th>Careful history, family history and physical examination, including screening for connective tissue disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-lead electrocardiogram</td>
</tr>
<tr>
<td>Echocardiogram including assessment of left and right ventricular and valve function</td>
</tr>
<tr>
<td>Exercise test to be considered for objective assessment of functional classification</td>
</tr>
</tbody>
</table>

**Careful counselling** including maternal risks for complications and mortality, information on choices of therapy (heparin versus Vitamin K), risk of miscarriage, risk of early delivery and small for gestational age and, when applicable, risk of fetal congenital defect (inheritance risk)
An approach to a peripartum woman presenting with a high risk condition or heart failure

**Important Questions**

- Is the patient known to have an underlying heart disease?
  - No: Follow diagnostic algorithm
  - Yes: Manage according to underlying disease

- Weeks of gestation?
  - <16 weeks: Pregnancy desired?
    - Yes: Early delivery?
    - No: Termination
  - >16 weeks: Can the patient be stabilized? Intervention needed?
    - Yes: Early delivery?
    - No: Termination

- In Heart Failure?
  - Yes: Manage according to underlying disease
  - No: Follow diagnostic algorithm

**Comorbidities? Aggravating factors?**
Manage according to underlying disease

Rheumatic heart disease (native valves/operated)
- Medical therapy
- Surgery/balloon valvotomy

Others:
- Marfan’s disease
- Cardiac sarcoidosis
- Constrictive pericarditis

Successfully operated:
- More imaging needed (e.g., MRI for coartation)?
- Residual defects?

Not operated:
- Single defects?
- Complex defects?

Cardiomyopathy

Congenital heart disease
2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy

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

Endorsed by: the International Society of Gender Medicine (IGM), the German Institute of Gender in Medicine (DGuSeGM), the European Society of Anaesthesiology (ESA), and the European Society of Gynecology (ESG)

Authors/Task Force Members: Vera Regitz-Zagrosek* (Chairperson) (Germany), Jolien W. Roos-Hesselink* (Co-Chairperson) (The Netherlands), Johann Bauersachs (Germany), Carina Blomström-Lundqvist (Sweden), Renata Cifkóvá (Czech Republic), Michele De Bonis (Italy), Bernard Iung (France), Mark Richard Johnson (UK), Ulrich Kintscher (Germany), Peter Kranke¹ (Germany), Irene Marthe Lang (Austria), Joao Morais (Portugal), Petronella G. Pieper (The Netherlands), Patrizia Presbitero (Italy), Susanna Price (UK), Giuseppe M. C. Rosano (UK/Italy), Ute Seeland (Germany), Tommaso Simoncini² (Italy), Lorna Swan (UK), Carole A. Warnes (USA)
What are contributing factors to poor outcome?
Contributing factor #1: Maternal Age


Global maternal mortality ratio in 1990 and 2013, by age. Shaded areas show 95% uncertainty intervals.
Contributing factor #2: Anemia? Fever? On medication? Underlying infection (e.g. HIV, malaria)? Sepsis?

Maternal adaptation to pregnancy and delivery

- Plasma volume by 40%
- Physiologic anaemia
- Cardiac output by 30 - 50%
- Transient LV dilatation
- Hypercoagulable state
- Cardiac output during delivery/postpartum
- Weeks to months for CO and SVR to normalize
Contributing factor #3:

Echocardiography: Left Ventricular Dysfunction often with Mitral Regurgitation and Pulmonary Hypertension
Tapse:
An index of RV function but also a predictor of mortality in cardiomyopathy!

Reduced TAPSE, signifying RV systolic dysfunction, is defined as value of ≤ 14 mm
General factors contributing to increased maternal and fetal risk in pregnant women with heart disease

- Maternal socioeconomic factors:
  - Age < 18 or Age > 35
  - Poor maternal education
  - Low household income
  - Long distance to appropriate care

- Health System factors:
  - Un-skilled health care workers
  - Lack of tools to make early diagnosis
  - In-appropriate referral algorithm
  - Long distances to appropriate care

- Maternal Health Factors:
  - Late presentation (> 20 weeks)
  - Pre-existing heart failure
  - Atrial Fibrillation
  - Anaemia

- Conditions listed at the Modified WHO stage II-IV
Fetal Outcome

1. Congenital heart disease
   - Risk of miscarriage is substantially increased
   - Prematurity, low birth weight/small for gestational age, offspring mortality linked to severity of disease
   - Recurrence of congenital heart disease (3-5%); in syndromes as e.g. Noonan syndrome (50%)

2. Rheumatic heart disease
   - Effects of anticoagulation with warfarin (foetal loss, warfarin embryopathy)
   - Prematurity, low birth weight/small for gestational age

3. Cardiomyopathies
   - Impaired utero-placental flow leads to increased foetal complication rates
   - Effects of medication that needs to be continued
Medical Management


Halpern et al, Use of Medication for Cardiovascular Disease During Pregnancy, JACC 2018:39:3165-3241
**Medical Management**

**Contributing factors**

- Medical
- Non Pregnancy
- Early Pregnancy
- Late Pregnancy
- Postpartum

**Figure 1:** Hemodynamic and Pharmacological Changes During Pregnancy

The pharmacokinetic and hemodynamic changes throughout pregnancy. (A) System based pharmacokinetic changes throughout pregnancy. (B) Hemodynamic changes diagram throughout pregnancy. CO = cardiac output; GFR = glomerular filtration rate; HR = heart rate; MAP = mean arterial pressure; RBC = red blood cell; SV = stroke volume; SVR = systemic vascular resistance; Vd = volume of distribution; VwF = Von Willebrand factor. Image in B adapted from Fuster V, Harrington RA, Narula J, Eapen ZJ, editors. Hurst's the Heart. 14th edition. New York, NY: McGraw Hill, 2017.
### Medical Management

**Halpern et al, Use of Medication for Cardiovascular Disease During Pregnancy, JACC 2018:39:3165-3241**

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#### TABLE 1 FDA’s Current Pregnancy, Lactation, and Reproductive Potential: Labeling for Human Prescription Drug and Biological Products

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pregnancy</strong></td>
<td>This subsection contains information on pregnancy, including labor and delivery.</td>
</tr>
<tr>
<td></td>
<td>Narrative summaries of the risks of a drug during pregnancy and discussions of the data supporting those summaries are required in labeling to provide more meaningful information for clinicians under the following subheadings:</td>
</tr>
<tr>
<td></td>
<td>- Pregnancy exposure registry: to inform health care providers of the availability of a pregnancy exposure registry for a product with contact information (e.g., a toll-free telephone number, web 178 site) needed to enroll in or to obtain information about the registry.</td>
</tr>
<tr>
<td></td>
<td>- Risk summary: If information on birth defects and miscarriage is available for the patient population for whom the drug is labeled, it must be included. When use of a drug is contraindicated during pregnancy, this information must be stated first.</td>
</tr>
<tr>
<td></td>
<td>- &quot;Structural abnormalities&quot; describes dysmorphology, which includes malformations, variations, deformations, and disruptions.</td>
</tr>
<tr>
<td></td>
<td>- &quot;Embryo-fetal and/or infant mortality&quot; describes developmental mortality, which includes miscarriage, stillbirth, and infant death (including neonatal death).</td>
</tr>
<tr>
<td></td>
<td>- &quot;Functional impairment&quot; describes functional toxicity, which includes such outcomes as deafness, endocrinopathy, neurodevelopmental effects, and impairment of reproduction.</td>
</tr>
<tr>
<td></td>
<td>- &quot;Alterations to growth&quot; describes such outcomes as growth restriction, excessive growth, and delayed and early maturations.</td>
</tr>
<tr>
<td><strong>Clinical considerations</strong></td>
<td>- Disease-associated maternal and/or embryo/fetal risk;</td>
</tr>
<tr>
<td></td>
<td>- Dose adjustments during pregnancy and the postpartum period;</td>
</tr>
<tr>
<td></td>
<td>- Maternal adverse reactions;</td>
</tr>
<tr>
<td></td>
<td>- Fetal/neonatal adverse reactions;</td>
</tr>
<tr>
<td></td>
<td>- Labor or delivery</td>
</tr>
<tr>
<td><strong>Data</strong></td>
<td>- Human data;</td>
</tr>
<tr>
<td></td>
<td>- Animal data</td>
</tr>
</tbody>
</table>

*FDA = U.S. Food and Drug Administration.*
Medical Management

Halpern et al, Use of Medication for Cardiovascular Disease During Pregnancy, JACC 2018;39:3165-3241. Adapted from Nishimura et al. JACC 2014; 63:e57-185

*SA Heart*

---

**Figure 2: Anticoagulation of Pregnant Patients With Mechanical Valves**

- **Pregnant Patient With Mechanical Valve**
  - **Class I**
  - **Class IIa**
  - **Class IIb**

- **Therapeutic anticoagulation with frequent monitoring (I)**

- **Baseline warfarin dose ≤5 mg/day**
  - **First trimester**
  - Continue warfarin with close INR monitoring (IIa)
    - OR
    - Dose-adjusted LMWH ≥2x/day (target anti-Xa level 0.8 U/mL to 1.2 U/mL 4-6 h post dose) (IIb)
      - OR
      - Dose-adjusted continuous infusion of UFH (with an aPTT at least 2x control) (IIb)

- **Baseline warfarin dose >5 mg/day**
  - **First trimester**
  - Dose-adjusted LMWH ≥2x/day (target anti-Xa level 0.8 U/mL to 1.2 U/mL 4-6 h post dose) (IIa)
    - OR
    - Dose-adjusted continuous infusion of UFH (with an aPTT at least 2x control) (IIa)

- **Second and third trimesters**
  - Warfarin to goal INR plus ASA 75 mg QD to 100 mg QD (I)
  - Before planned vaginal delivery
    - Discontinue warfarin and initiate dose-adjusted continuous infusion of UFH (with an aPTT at least 2x control) (I)

---

aPTT = activated partial thromboplastin time; ASA = aspirin; INR = international normalized ratio; LMWH = low molecular weight heparin; QD = once daily; UFH = unfractionated heparin. Adapted from Nishimura et al. (143).
### Medical Management

#### High Risk Pregnancy

**What one needs to know**

**Medical Management**

---

**Central Illustration: Cardiovascular Medications in Pregnancy**

#### Arrhythmias

- Adenosine
- Metoprolol/propranolol
- Digoxin
- Lidocaine
- Verapamil
- Diltiazem
- Procainamide
- Sotalol
- Flecainide
- Propafenone

- Amiodarone

* May be used if other therapies fail.

#### Hypertension

- Labetalol
- Nifedipine
- Alpha-methyl(dopa oral)
- Hydralazine
- Nitroglycerin
- Nitroprusside
- Isosorbide dinitrate
- Amlodipine
- Furosemide
- Hydrochlorothiazide
- Clonidine

#### Heart Failure

- Metoprolol
- Carvedilol
- Furosemide
- Bumetanide
- Dopamine
- Dobutamine
- Norepinephrine
- Hydralazine
- Nitroglycerin
- Isosorbide dinitrate
- Torsemide
- Metolazone

#### Pulmonary Hypertension

- Iloprost
- Epoprostenol
- Sildenafil
- Treprostinil

#### Contraindicated in Pregnancy

- Atenolol
- ACE-I class
- ARB class
- Aldosterone antagonists
- Statin class
- DOACs
- ERAs (e.g. bosentan)

---

### Anticoagulants/Antiplatelets/Thrombolytics

- **Anticoagulants**
  - Warfarin
  - Unfractionated Heparin
  - Enoxaparin
  - Fondaparinux
  - Argatroban
  - Bivalirudin
  - Antiplatelets
  - Aspirin (low dose)
  - Clopidogrel
  - Prasugrel
  - Ticagrelor
  - Thrombolytics
  - Alteplase
  - Streptokinase

---


- Safety in pregnancy
- FDA category
- Safety in lactation
- Used also for fetal treatment

- Considered safe
- Limited data/to be used with caution
- Contraindicated
- Conflicting data/unknown
Cardiac medication during pregnancy, data from the ROPAC

Birth weight in patients with and without beta-blockers per WHO class adjusted for gestational age, smoking, fetal sex, maternal age, diabetes and pre-eclampsia.

Results

48% of the newborns exposed to ACE-Is and 87% of the newborns exposed to ARBs did exhibit any complications (P < 0.0001)
What one needs to know about Peripartum Cardiomyopathy

- Idiopathic form of cardiomyopathy
- Presenting with heart failure towards the end of pregnancy, or in the months following delivery
- No other causes of heart failure are found
- A diagnosis of exclusion
- Left ventricular ejection fraction usually below 40%
Peripartum cardiomyopathy (PPCM) is a potentially life-threatening condition typically presenting as heart failure with reduced ejection fraction (HFrEF) in the last month of pregnancy or in the months following delivery in women without another known cause of heart failure.

This updated position statement (June 2019) summarizes the knowledge about pathophysiological mechanisms, risk factors, clinical presentation, diagnosis and management of PPCM.
- As shortness of breath, fatigue and leg oedema are common in the peripartum period, a high index of suspicion is required to not miss the diagnosis.
- Measurement of natriuretic peptides, electrocardiography and echocardiography are recommended to promptly diagnose or exclude heart failure/PPCM.

**Figure 1:** Diagnostic pathway in patients with suspected peripartum cardiomyopathy (PPCM). BNP, B-type natriuretic peptide; ECG, electrocardiogram; HF, heart failure; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; RV, right ventricular.
Suspected acute PPCM*

Natriuretic peptides, ECG, chest X-ray, and echocardiography

Natriuretic peptides↑**
and LVEF <45%

Acute PPCM likely

Exclude overt pre-existing heart disease
(e.g. chemotherapy-induced cardiomyopathy, congenital or valvular heart disease, hypertrophic cardiomyopathy)

Natriuretic peptides↑
and LVEF ≥45%

Consider other cardiac and extracardiac origin of symptoms
(e.g. pulmonary embolism, amniotic fluid embolism, isolated RV dysfunction, hypertensive disorders of pregnancy, eclampsia, sepsis)

Natriuretic peptides normal and LVEF ≥45%

Consider extracardiac origin of symptoms
(e.g. anaemia, pneumonia, renal disease, hypertensive disorders of pregnancy, eclampsia, depression, physiological changes)

* Symptoms during end of pregnancy or months following delivery: dyspnoea, orthopnoea, peripheral oedema, chest pain, dizziness, palpitations, fatigue, depression, cough

** Cut-off for acute HF: NT-proBNP >300 pg/ml, BNP >100 pg/ml
Table 2. Diagnostic tests that are recommended for the diagnosis of peripartum cardiomyopathy at initial diagnosis and at follow-up visits

<table>
<thead>
<tr>
<th>Time After Diagnosis</th>
<th>Clinical examination</th>
<th>ECG</th>
<th>Natriuretic peptides</th>
<th>Echocardiography</th>
<th>Chest X-ray</th>
<th>Cardiac MRI</th>
<th>CT scan</th>
<th>Coronary angiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis of PPCM</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>(X)(a)</td>
<td>(X)(a)</td>
<td>(X)(a)</td>
</tr>
<tr>
<td>4-6 weeks after diagnosis</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>(X)(b)</td>
<td>(X)(b)</td>
<td>(X)(b)</td>
</tr>
<tr>
<td>3 months after diagnosis</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 months after diagnosis</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>(X)(b)</td>
</tr>
<tr>
<td>12 months after diagnosis</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>(X)(b)</td>
<td>(X)(b)</td>
<td>(X)(b)</td>
</tr>
<tr>
<td>18 months after diagnosis</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Annually for at least 5 years after diagnosis (especially if not fully recovered)</td>
<td>X</td>
<td>X</td>
<td>Xa</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Generally, an individual approach is recommended depending on the severity of the disease and/or potential differential diagnoses.

*CT, computed tomography; ECG, electrocardiogram; MRI, magnetic resonance imaging; PPCM, peripartum cardiomyopathy.

\(a\) May be considered depending on costs and local availability.

\(b\) May be considered depending on the clinical presentation and/or differential diagnoses.

- PPCM is associated with high morbidity and mortality, but also with a high probability of partial and often full recovery.

- Use of guideline-directed pharmacological therapy for HFrEF is recommended in all patients respecting contraindications during pregnancy/lactation.
A recent study identified a long QTc interval at baseline which was found in almost 50% of the patients, and tachycardia as predictors of poor outcome in PPCM (Hoevelmann et al, Int J Cardiol, 2019).
<table>
<thead>
<tr>
<th>Differential diagnoses of peripartum cardiomyopathy</th>
<th>History</th>
<th>Onset</th>
<th>Biomarkers</th>
<th>Echocardiography/cardiac MRI</th>
<th>Differentiation from PPCM</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPCM</td>
<td>No known cardiac disease, no HF signs and/or symptoms prior pregnancy</td>
<td>Towards the end of pregnancy and the months following delivery</td>
<td>Elevated natriuretic peptides</td>
<td>Reduced systolic LV function, LVEF &lt; 45%</td>
<td>–</td>
</tr>
<tr>
<td>Myocarditis</td>
<td>Prior viral infection (e.g. respiratory)</td>
<td>Acute or subacute onset after viral infection</td>
<td>Elevated troponin, elevated CRP</td>
<td>Normal or reduced systolic LV function, typical myocardial late gadolinium enhancement pattern, pericardial effusion</td>
<td>Cardiac MRI (LE pattern), myocardial biopsy</td>
</tr>
<tr>
<td>Pre-existing idiopathic/ familial dilated or acquired cardiomyopathy</td>
<td>HF signs and/or symptoms and/or known heart disease prior pregnancy</td>
<td>During second trimester of pregnancy</td>
<td>Elevated natriuretic peptides</td>
<td>Reduced systolic LV function, RV dysfunction possible, typical myocardial LE pattern (DCM)</td>
<td>History, echocardiography, cardiac MRI (LE pattern)</td>
</tr>
<tr>
<td>Takotsubo syndrome</td>
<td>Chest pain, very stressful delivery or emergency due to foetal complications</td>
<td>Acute onset, during delivery or immediately after delivery</td>
<td>Elevated natriuretic peptides</td>
<td>Regional wall motion abnormalities with typical anatomical patterns</td>
<td>History, echocardiography</td>
</tr>
<tr>
<td>Pregnancy-associated myocardial infarction</td>
<td>Chest pain, epigastric pain</td>
<td>Acute onset, during pregnancy or immediately after delivery</td>
<td>Elevated troponin</td>
<td>Regional wall motion abnormalities, ischaemic myocardial scar</td>
<td>History, ECG, coronary angiography, cardiac MRI (LE pattern)</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>Chest pain, unilateral leg swelling, acute dyspnoea</td>
<td>Acute onset during pregnancy or after delivery</td>
<td>Elevated natriuretic peptides and/or troponin, elevated D-dimer</td>
<td>RV dysfunction, RV dilatation, LV function usually normal</td>
<td>Computed tomography, VQ scan</td>
</tr>
<tr>
<td>Amniotic fluid embolism</td>
<td>Chest pain during/immediately after delivery, acute dyspnoea</td>
<td>Acute onset during delivery or immediately after delivery</td>
<td>Elevated natriuretic peptides possible</td>
<td>Reduced RV systolic function, RV dilatation</td>
<td>History, echocardiography</td>
</tr>
<tr>
<td>Hypertensive heart disease/severe pre-eclampsia</td>
<td>Pre-existing or new-onset hypertension, proteinuria</td>
<td>During second trimester of pregnancy</td>
<td>Elevated natriuretic peptides</td>
<td>LV hypertrophy, diastolic dysfunction, transient LV dysfunction</td>
<td>History, echocardiography</td>
</tr>
<tr>
<td>Hypertrophic cardiomyopathy</td>
<td>Familial predisposition</td>
<td>During second trimester of pregnancy</td>
<td>Elevated natriuretic peptides</td>
<td>LV hypertrophy, typical myocardial late enhancement pattern, LVOTO (HOCM)</td>
<td>History, echocardiography, cardiac MRI (LE pattern)</td>
</tr>
<tr>
<td>HIV/AIDS cardiomyopathy</td>
<td>HIV infection, AIDS</td>
<td>During second trimester of pregnancy</td>
<td>Elevated natriuretic peptides</td>
<td>Reduced systolic LV function, LV/RV often not dilated</td>
<td>HIV serology/test</td>
</tr>
<tr>
<td>Pre-existing (unknown) congenital heart disease</td>
<td>HF signs and/or symptoms prior pregnancy, known heart disease, prior cardiac surgery</td>
<td>During second trimester of pregnancy</td>
<td>Elevated natriuretic peptides</td>
<td>(Corrected) congenital heart defects, cardiac shunts</td>
<td>History, echocardiography</td>
</tr>
<tr>
<td>Pre-existing valvular heart disease</td>
<td>HF signs and/or symptoms prior pregnancy, known heart disease</td>
<td>During second trimester of pregnancy</td>
<td>Elevated natriuretic peptides</td>
<td>Valvular stenosis or regurgitation, prosthetic heart valves</td>
<td>History, echocardiography</td>
</tr>
</tbody>
</table>

AIDS, acquired immunodeficiency syndrome; CRP, C-reactive protein; DCM, dilated cardiomyopathy; ECG, electrocardiogram; HOCM, hypertrophic obstructive cardiomyopathy; HF, heart failure; HIV, human immunodeficiency virus; LE, late enhancement; LV, left ventricular; LVEF, left ventricular ejection fraction; LVOTO, left ventricular outflow tract obstruction; MRI, magnetic resonance imaging; PPCM, peripartum cardiomyopathy; RV, right ventricular; VQ, ventilation–perfusion.
Pathogenesis of PPCM and novel therapeutic options

Sliwa, Lancet 2016; 388: e28–36

PPCM = peripartum cardiomyopathy. PRL = prolactin. miR = micro RNA. ROS = reactive oxygen species. NT-proBNP = N-terminal pro-b-type natriuretic peptide. MnSOD = manganese superoxide dismutase. STAT3 = signal transducer and activator of transcription 3. PGC-1α = peroxisome proliferator-activated receptor γ coactivator 1-α. sFlt = soluble fms-like tyrosine kinase. VEGF = vascular endothelial growth factor.

The oxidative stress-mediated cleavage of the hormone prolactin into a cardiotoxic fragment has been identified as a driver of PPCM pathophysiology. Pharmacological blockade of prolactin release using bromocriptine as a disease-specific therapy in addition to standard therapy for heart failure treatment has shown promising results in clinical trials.
What is new in the management of PPCM?

In patients with pulmonary embolism, thrombolytic therapy is recommended only in severe hypotension or shock. In women at high risk for thrombo-embolism, it is recommended to convert LMWH to UFH at least 36 h prior to delivery and stop the UFH infusion 4–6 h prior to anticipated delivery. aPTT should be normal before regional anaesthesia (IC).

In women at low risk for thrombo-embolism on therapeutic LMWH, induction or caesarean section is recommended to be performed 24 h after the last dose of LMWH (IC).

In women considering pregnancy and requiring heart valve surgery, it is recommended to choose the prosthesis in consultation with a pregnancy heart team (IC).

It is recommended to manage pregnancy in women with mechanical heart valves in a centre with a pregnancy heart team (IC).

In treatment-naïve pregnant PAH patients, initiating treatment should be considered (IIaC).

In patients with (history of) aortic dissection, caesarean delivery should be considered (IIaC).

Beta-blocker therapy throughout pregnancy should be considered in women with Marfan syndrome and other heritable thoracic aortic diseases (IIaC).

Induction of labour should be considered at 40 weeks gestation in all women with cardiac disease (IIaC).

In patients with PPCM, bromocriptine treatment may be considered to stop lactation and enhance recovery (LV function) (IIbB).

Pregnancy is not recommended in patients with vascular Ehlers-Danlos syndrome (IIIC).

Breastfeeding is not recommended in mothers who take antiplatelet agents other than low-dose aspirin (from section 7, see section 12) (IIIC).

New concepts

Enforcing mWHO classification of maternal risk.

Introduction of the pregnancy heart team.

More attention for assisted reproductive therapy.

Discussion of the use of bromocriptine in PPCM.

Introduction of specific levels of surveillance based on low/medium/high risk for arrhythmia with haemodynamic compromise at delivery.

New information on pharmacokinetics in pregnancy, more detailed information on pharmacodynamics in animal experiments on all drugs (Supplementary Data)

Perimortem caesarean section is discussed.

Advice on contraception and the termination of pregnancy in women with cardiac disease is now provided.
Breastfeeding in patients with any form of heart failure is controversial. According to the 2018 ESC guidelines for the management of cardiovascular diseases during pregnancy patients with severe heart failure preventing lactation may be considered due to the high metabolic demands of lactation and breastfeeding (class IIb recommendation).
CASE STUDY IV:
Heart failure during pregnancy

Discussion

What is the diagnosis of our patient?

What investigations should be done?

How should that women be managed?

What pharmacological therapy be started?
Typical 2: Overview of different clinical scenarios in patients with peripartum cardiomyopathy (results from diagnostic tests and recommended monitoring/treatment options are depicted according to disease severity. ECG, electrocardiogram; ECMO, extracorporeal membrane oxygenation; HF, heart failure; HFU, heart failure unit; ICU, intensive care unit; IMC, intermediate care unit; LVEF, left ventricular ejection fraction; RV, right ventricular; SBP, systolic blood pressure.\textsuperscript{a} Bromocriptine may be considered in PPCM patients (class Iib recommendation) and should be accompanied by at least prophylactic anticoagulation.

- **Our patient would belong to GROUP Moderate PPCM**

- **There are no specific recommendations how long medication on standard heart failure therapy should be continued. However, Ace-inhibitors and Beta-blockers should at least be continued for 2 years even in patients with improved cardiac function.**

- **Subsequent pregnancy should be avoided for at least 2 years irrespective of left ventricular function and is contraindicated if EF < 35%.**
Mild PPCM

- **Clinical presentation**
  - Subacute heart failure
  - Haemodynamic stability

- **ECG**
  - No specific changes

- **Chest X-ray**
  - Pulmonary congestion, may also be normal

- **Natriuretic peptides**
  - ↑

- **Echocardiography**
  - LVEF 30-45%

- **Therapy**
  - Oral HF drugs
  - Oral diuretics in case of fluid overload
  - Consider bromocriptine for 1 week

Moderate PPCM

- **Clinical presentation**
  - Acute heart failure
  - Haemodynamic stability
  - Respiratory insufficiency

- **ECG**
  - No specific changes, often tachycardia

- **Chest X-ray**
  - Pulmonary congestion, enlarged cardiac silhouette

- **Natriuretic peptides**
  - ↑↑

- **Echocardiography**
  - LVEF 20-35%

- **Therapy**
  - Diuretics i.v.
  - Consider vasorelaxants if SBP >110 mmHg
  - Supplemental O₂, non-invasive ventilation if necessary
  - Avoid inotropes/catecholamines
  - Consider bromocriptine for 8 weeks if LVEF <25%
  - Oral HF drugs

Severe PPCM

- **Clinical presentation**
  - Cardiogenic shock
  - Haemodynamic instability
  - Respiratory insufficiency

- **ECG**
  - No specific changes, often tachycardia

- **Chest X-ray**
  - Pulmonary congestion, enlarged cardiac silhouette, pleural effusion

- **Natriuretic peptides**
  - ↑↑

- **Echocardiography**
  - LVEF <25%, RV dysfunction and dilatation possible

- **Therapy**
  - Diuretics i.v.
  - Inotropes/catecholamines if needed
  - Invasive ventilation
  - Mechanical circulatory support (Impella and/or ECMO)
  - Consider bromocriptine for 8 weeks, up titration depending on prolactin levels
  - Oral HF drugs after stabilization
Conclusions

Each woman with substantial cardiac disease & pregnancy is unique

Effect on mother and fetus needs to be balanced

A multi-disciplinary approach including cardiologist, obstetricians, anaesthesists, cardiothoracic surgeons and others should be facilitated and will improve outcome

Understanding the precursors and preventing heart failure in pregnancy will have the highest impact