HeFSSA Practitioners Program 2019
"Challenges in Heart Failure Management"

- 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

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Introduction to Heart Failure in Pregnancy

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 post partum 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.

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Contributors to Maternal Death in South Africa

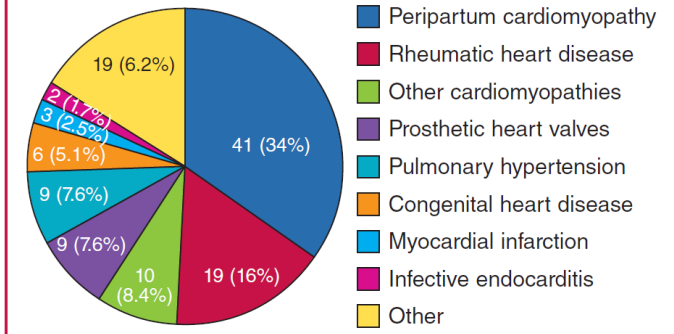
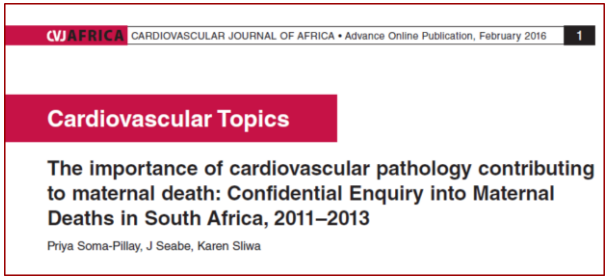


Fig. 3. Cardiovascular conditions contributing to cardiac death (n = 118).



PPCM (34%) and complications of RHD (25.3%) were the most important causes of heart failure and maternal death.

Factors contributing to death for the 2 major disease groups			
	Whole group	Peripartum cardiomyopathy	Rheumatic heart disease
Avoidable factors	n (%)	n (%)	n (%)
Patient delay in seeking help	49 (41.5)	16 (39.0)	16 (45.7)
Lack of expertise by medical staff managing case	35 (29.7)	16 (39.0)	12 (34.3)
Delay in referral to appropriate level of care	31 (26.3)	13 (31.7)	8 (22.9)
Delay in appropriate action	43 (36.4)	15 (36.6)	15 (42.9)

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CASE STUDY I

Heart failure during pregnancy

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.

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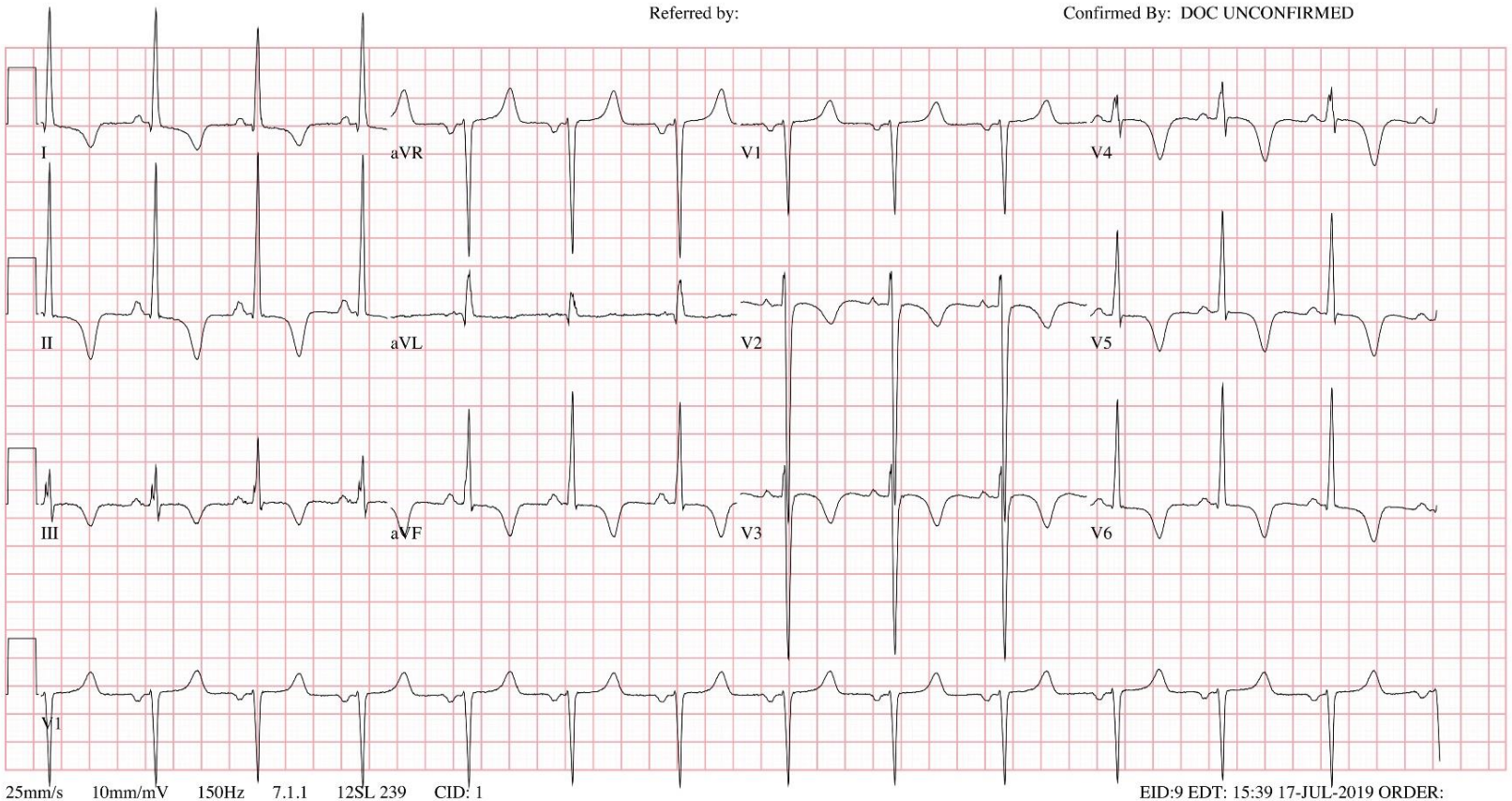
CASE STUDY II

Heart failure during pregnancy



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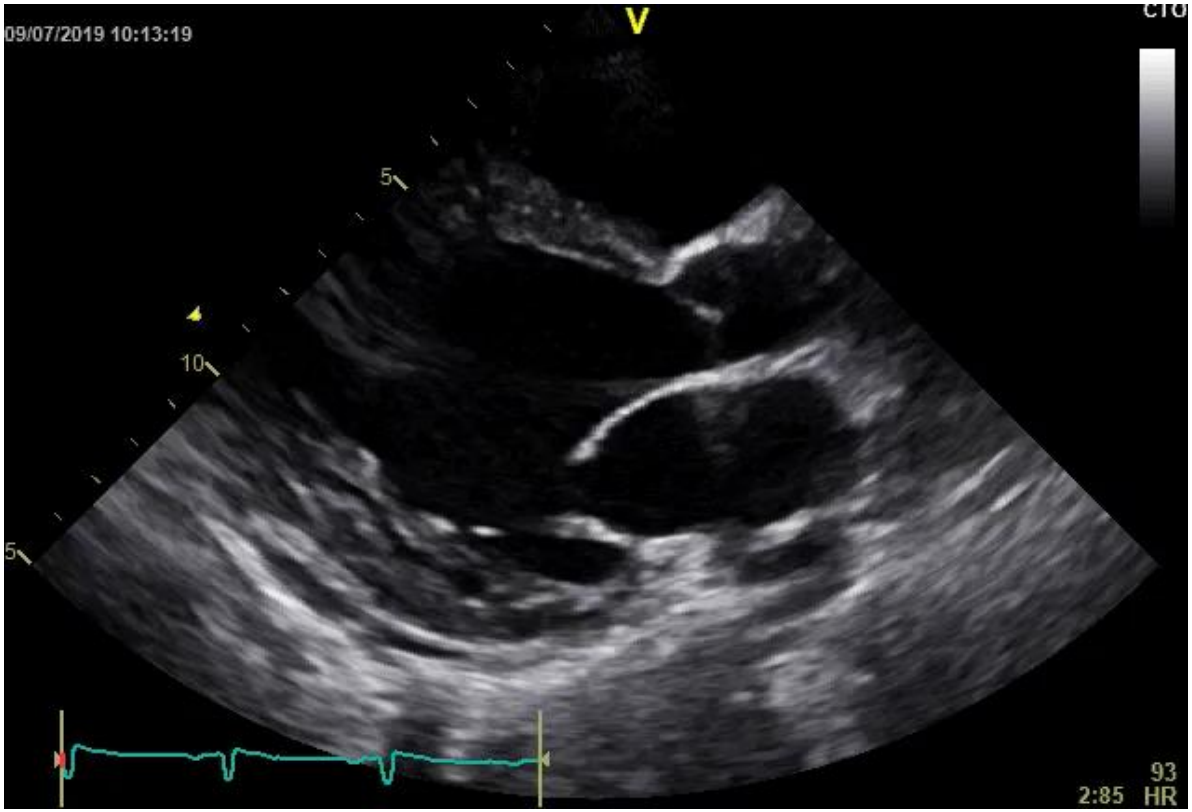
CASE STUDY II:

Heart failure during pregnancy

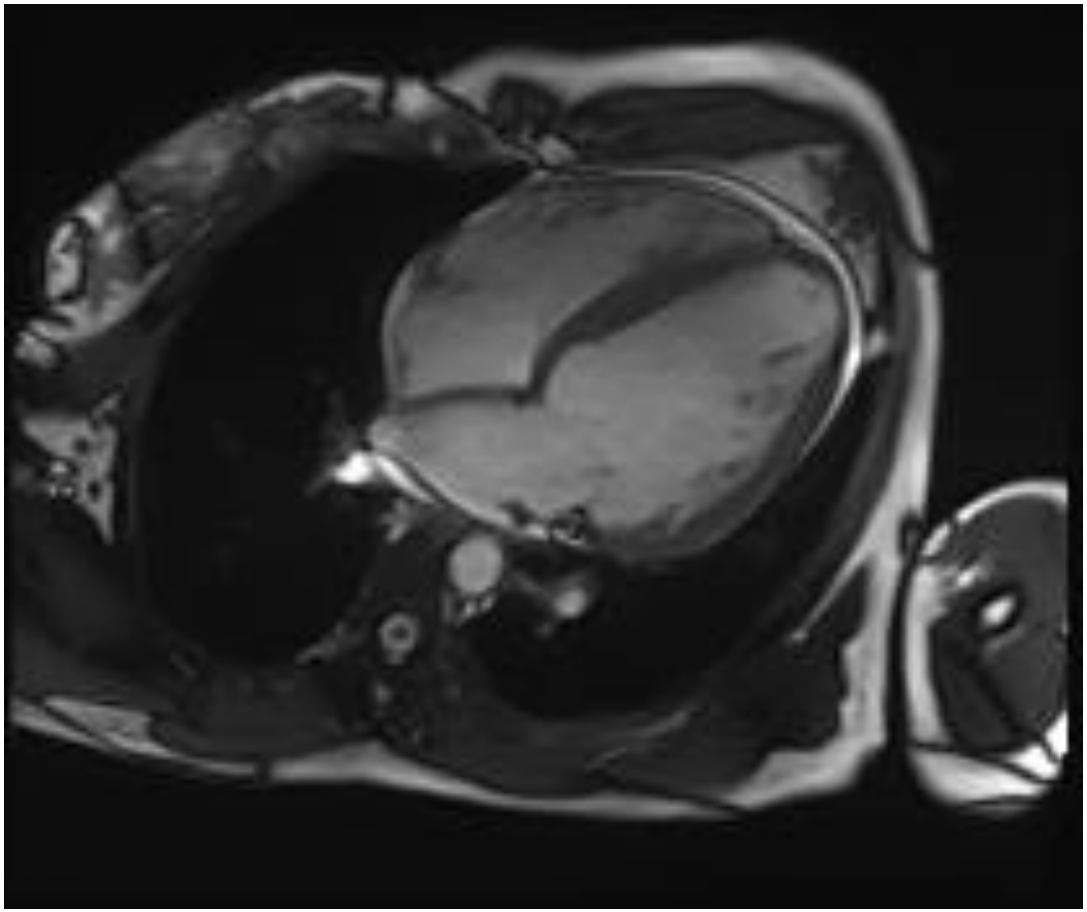
Cardiac ultrasound:



CASE STUDY III:

Heart failure during pregnancy

Cardiac MRI



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Outline

- A practical approach
- Geographic location
- High risk pregnancy
- Contributing factors
- Medical management
- Peripartum Cardiomyopathy
- Conclusions

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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.

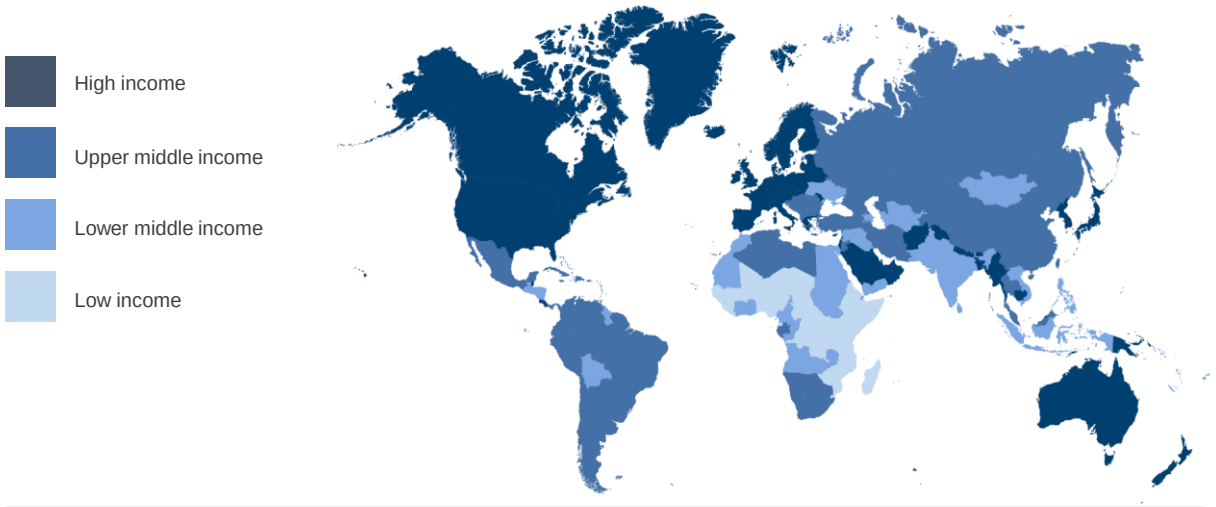
2

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

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Modified WHO Classification of Maternal Cardiovascular Risk

Regitz-Zagrosek et al. 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy.. Eur Heart J. 2018;39:3165-3241

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

Regitz-Zagrosek et al. 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy.. Eur Heart J. 2018;39:3165-3241

Conditions in which pregnancy risk is WHO IV (pregnancy contraindicated) maternal cardiac event rate: 40-100%
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 ascending aorta > 45 mm Bicuspid aortic valve with ascending aortic diameter >50 mm
Native severe coarctation
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.

Careful history, family history and physical examination, including screening for connective tissue disorders
12-lead electrocardiogram
Echocardiogram including assessment of left and right ventricular and valve function
Exercise test to be considered for objective assessment of functional classification
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)

European Heart Journal Advance Access published April 29, 2015

European Heart Journal
doi:10.1093/eurheartj/ehv141

REVIEW

Prevention

Contraception and cardiovascular disease

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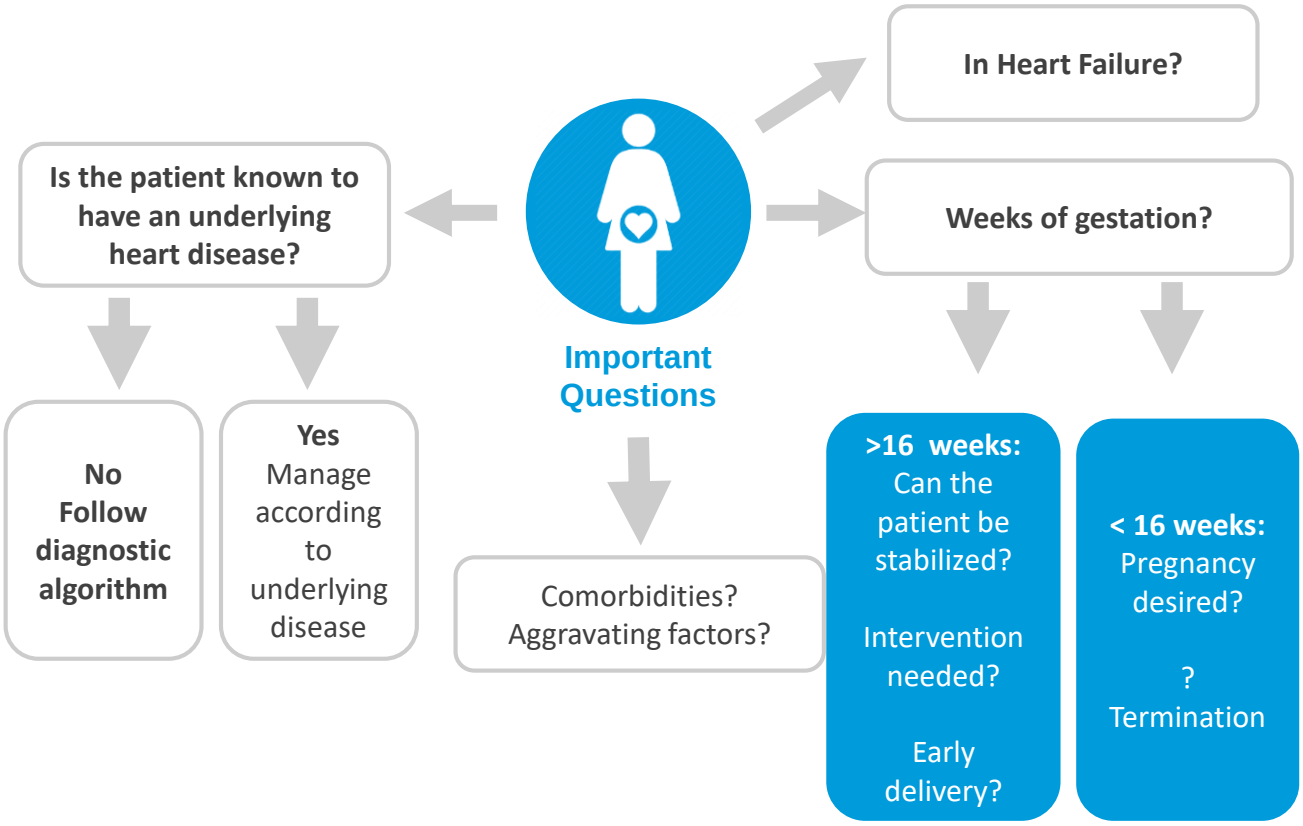
An approach to a peripartum woman presenting with a high risk condition or heart failure



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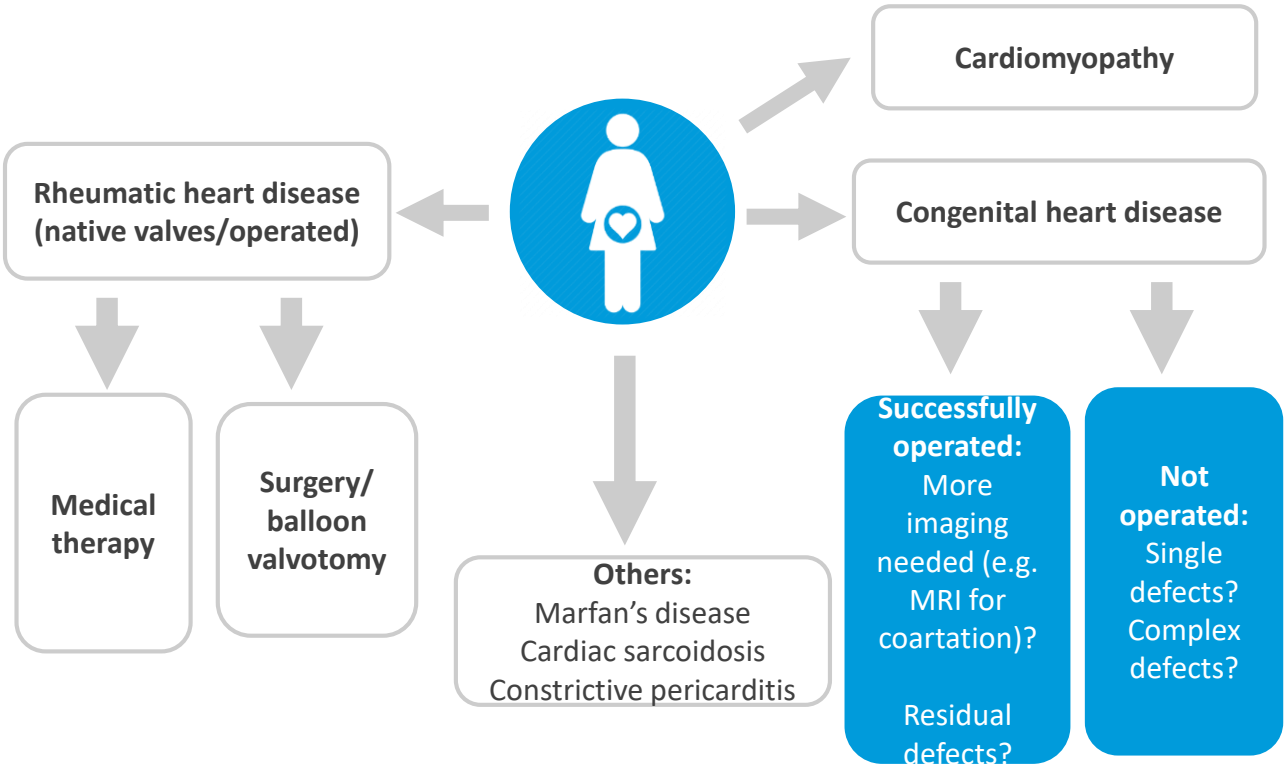
Manage according to underlying disease



Seek Guidance - multidisciplinary team!

ESC European Society of Cardiology

European Heart Journal (2018) **00**, 1–83
doi:10.1093/eurheartj/ehy340

ESC GUIDELINES

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 (DGesGM), 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 Cífková (Czech Republic), Michele De Bonis (Italy), Bernard Iung (France), Mark Richard Johnson (UK), Ulrich Kintscher (Germany), Peter Kranke[1] (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 Simoncini[2] (Italy), Lorna Swan (UK), Carole A. Warnes (USA)

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What are contributing factors to poor outcome?

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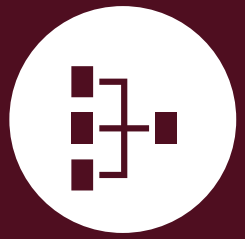
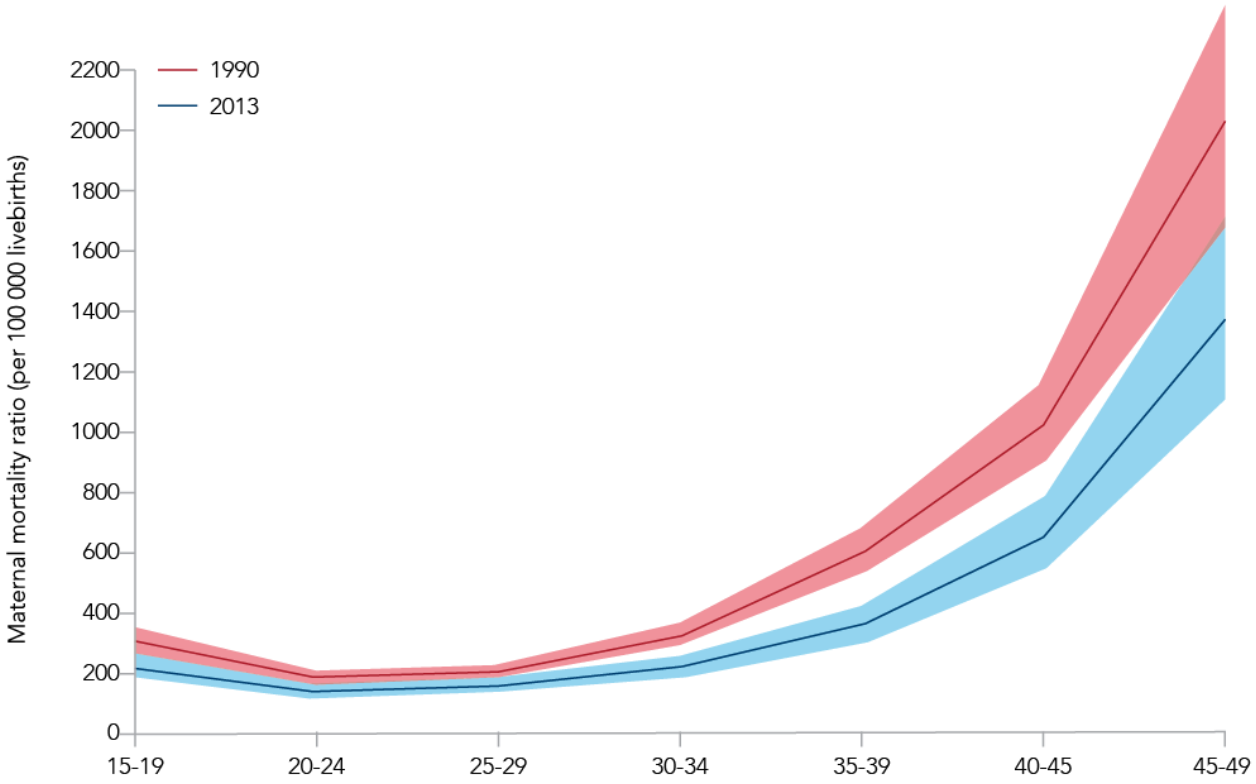
Contributing factor #1:

Maternal Age



Kassebaum NJ, Bertozzi-Villa A, Coggeshall MS, Sliwa K, Lozano R, et al. Global, regional, and national levels and causes of maternal mortality during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014



Global maternal mortality ratio in 1990 and 2013, by age. Shaded areas show 95% uncertainty intervals

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Contributing factor #2:

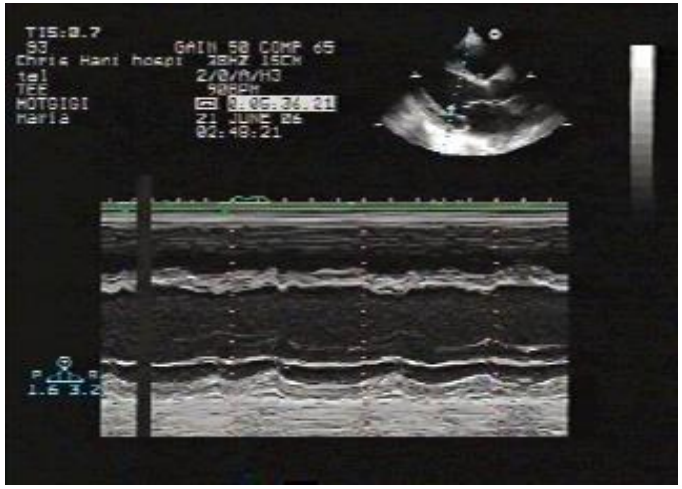
Anemia? Fever? On medication? Underlying infection (e.g. HIV, malaria)? Sepsis?

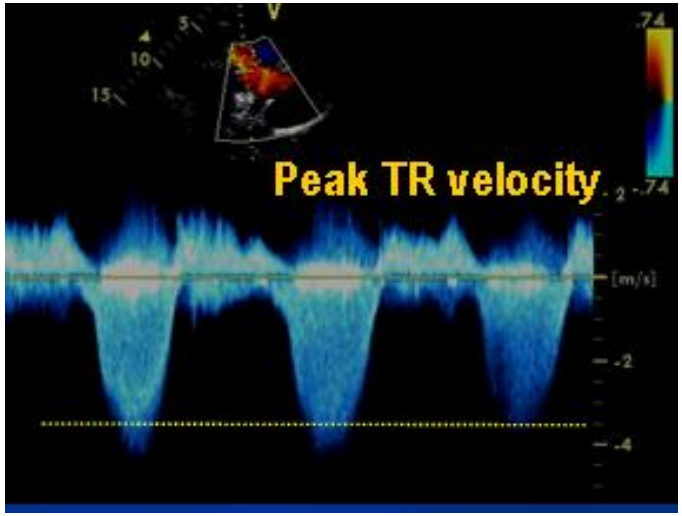
Maternal adaptation to pregnancy and delivery

Plasma volume by **40%**	Physiologic anaemia	Cardiac output by **30 - 50%**	Cardiac output during delivery/ postpartum
Systemic Vascular resistance	Transient LV dilatation	Hypercoagulable state	Weeks to months for CO and SVR to normalize

Contributing factor #3:

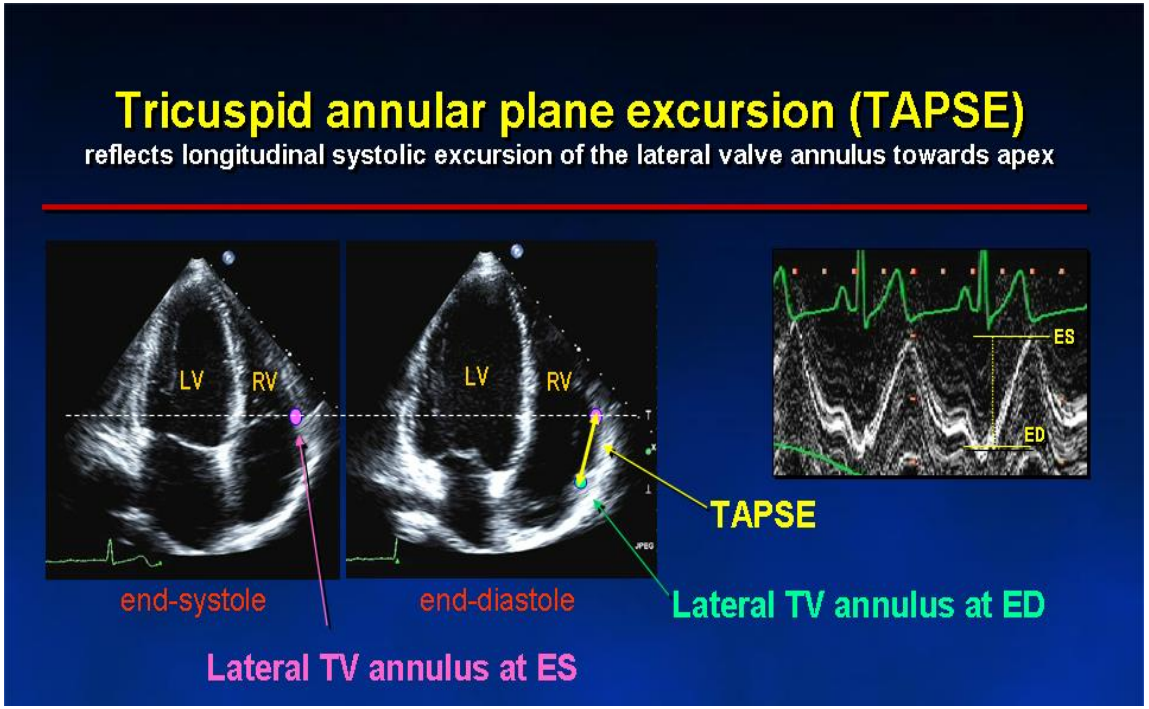
Echocardiography: Left Ventricular Dysfunction often with Mitral Regurgitation and Pulmonary Hypertension





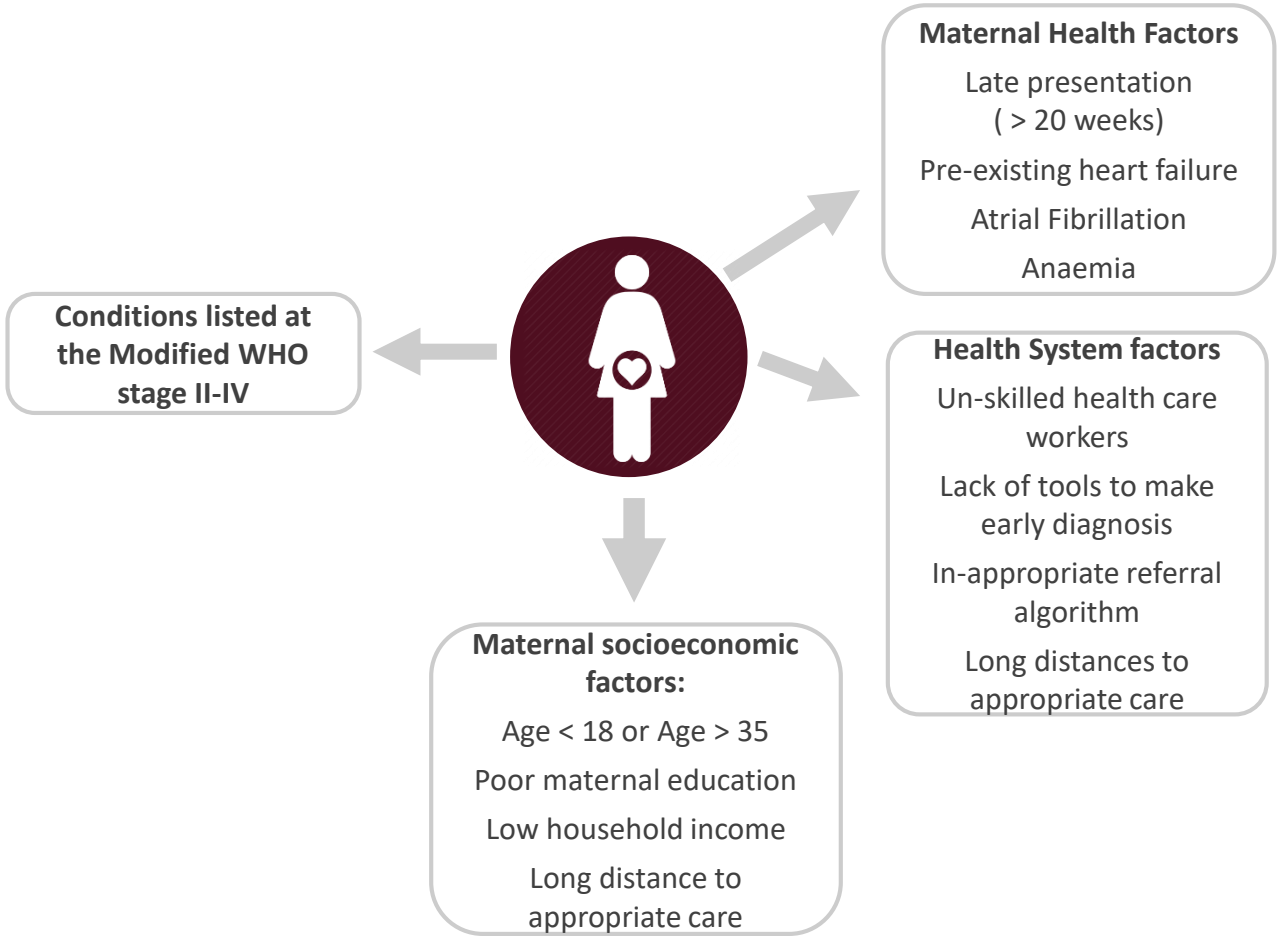
Tapse:

An index of RV function but also a predictor of mortality in cardiomyopathy!

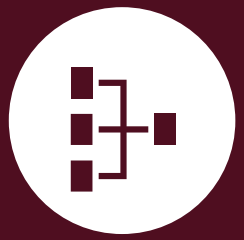


Reduced TAPSE, signifying RV systolic dysfunction, is defined as value of ≤ 14 mm

General factors contributing to increased maternal and fetal risk in pregnant women with heart disease



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

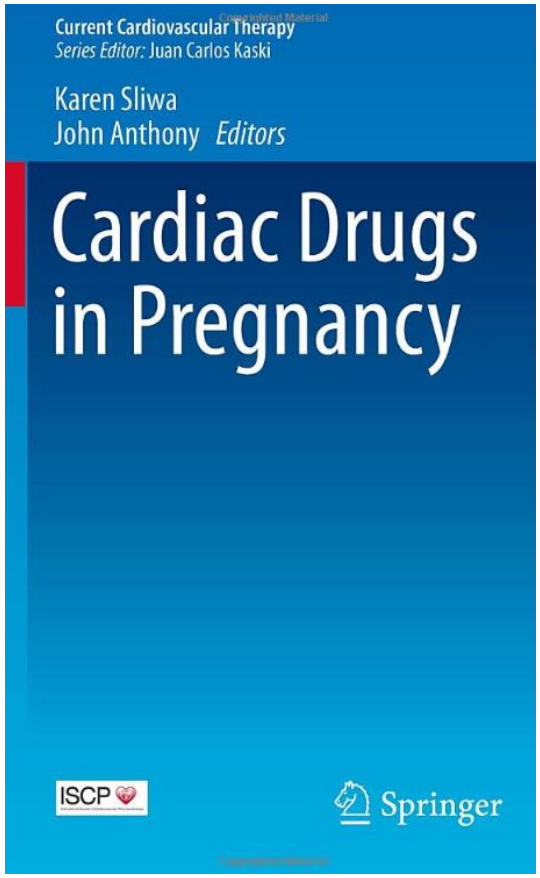
Impaired utero-placental flow leads to increased foetal complication rates

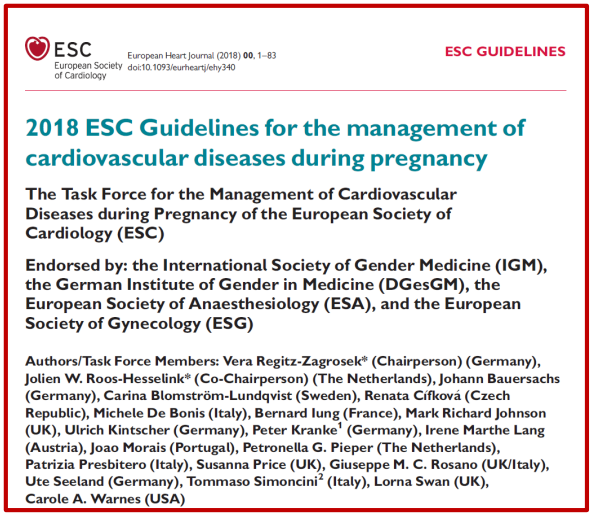
Effects of medication that needs to be continued

Medical Management

Regitz-Zagrosek et al. 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy.. Eur Heart J. 2018;39:3165-3241

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





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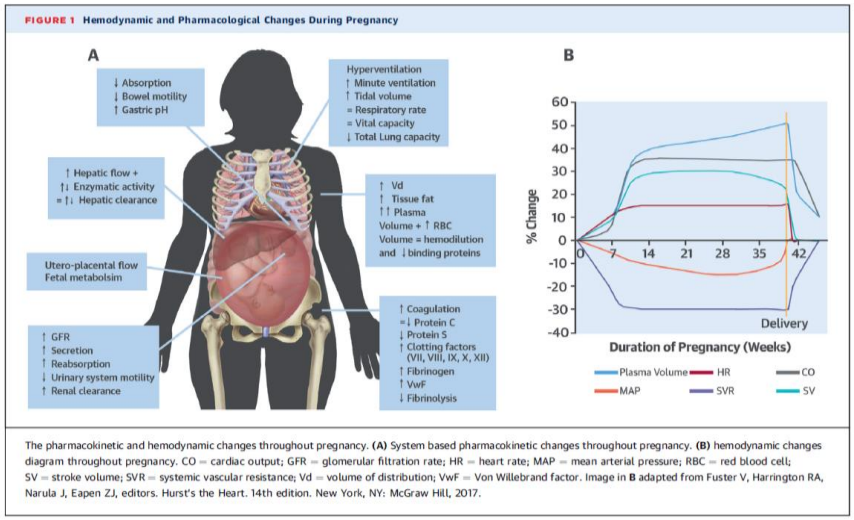
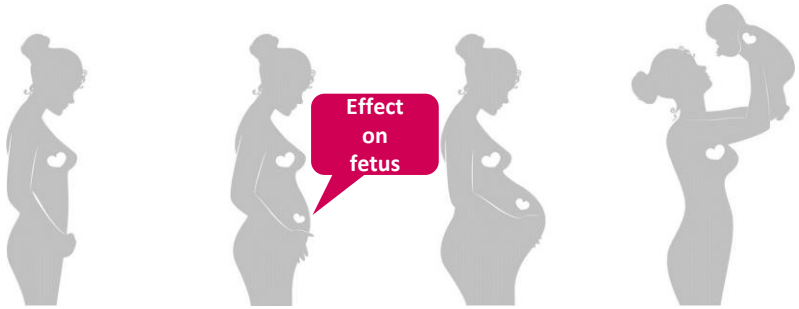


The pharmacokinetic and hemodynamic changes throughout pregnancy. **(A)** System based pharmacokinetic changes throughout pregnancy. **(B)** hemodynamic changes diagram throughout pregnancy. CO = cardiac output; GFR = glomerular filtration rate; HR = heart rate; MAP = mean arterial pressure; RBC = red 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.



Non Pregnant | Early Pregnancy | Late Pregnancy | Postpartum

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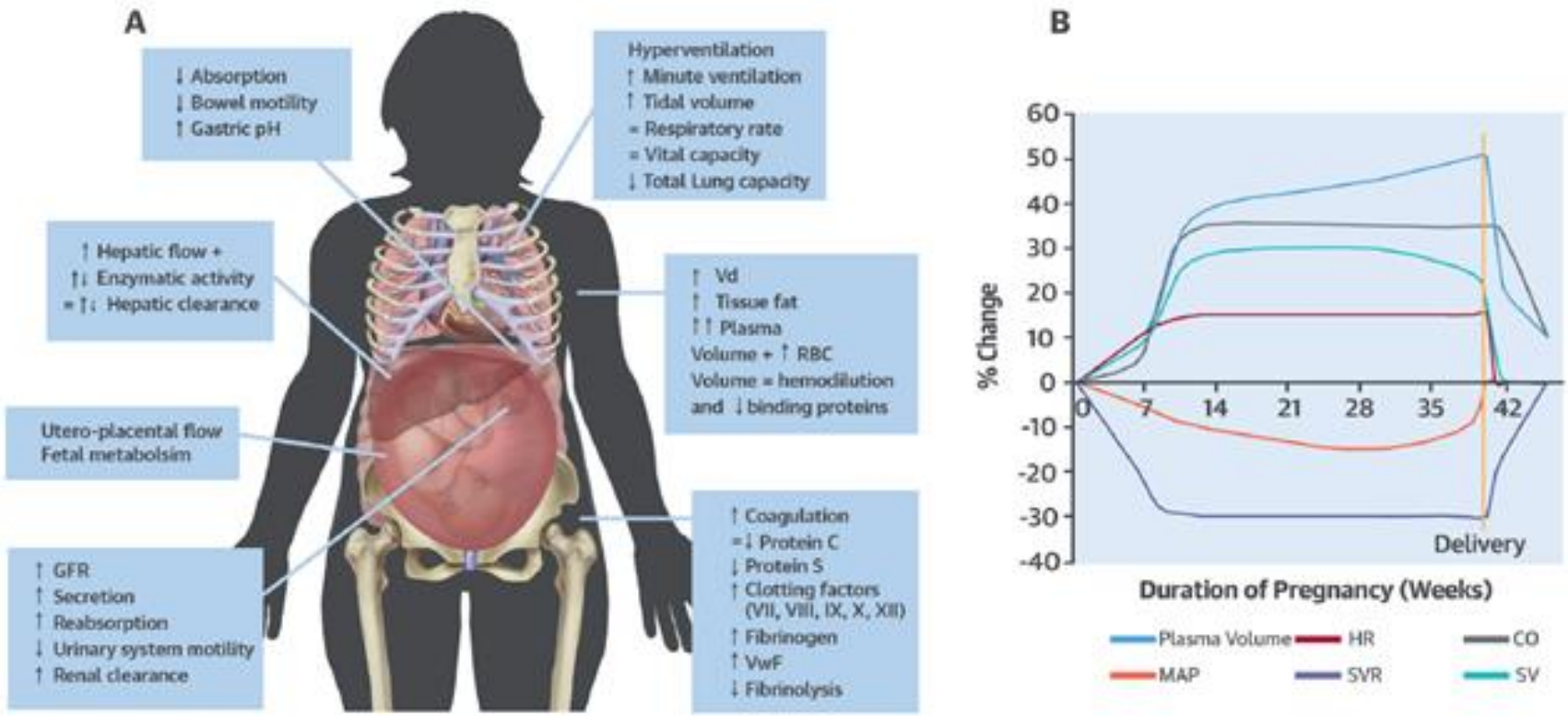
FIGURE 1 Hemodynamic and Pharmacological Changes During Pregnancy



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.

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

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

Pregnancy

This subsection contains information on pregnancy, including labor and delivery.

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:

- 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.
- 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.
  - "Structural abnormalities" describes dysmorphology, which includes malformations, variations, deformations, and disruptions.
  - "Embryo-fetal and/or infant mortality" describes developmental mortality, which includes miscarriage, stillbirth, and infant death (including neonatal death).
  - "Functional impairment" describes functional toxicity, which includes such outcomes as deafness, endocrinopathy, neurodevelopmental effects, and impairment of reproduction.
  - "Alterations to growth" describes such outcomes as growth restriction, excessive growth, and delayed and early maturations.
- Clinical considerations
  - Disease-associated maternal and/or embryo/fetal risk;
  - Dose adjustments during pregnancy and the postpartum period;
  - Maternal adverse reactions;
  - Fetal/neonatal adverse reactions;
  - Labor or delivery
- Data
  - Human data;
  - Animal data

FDA = U.S. Food and Drug Administration.

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

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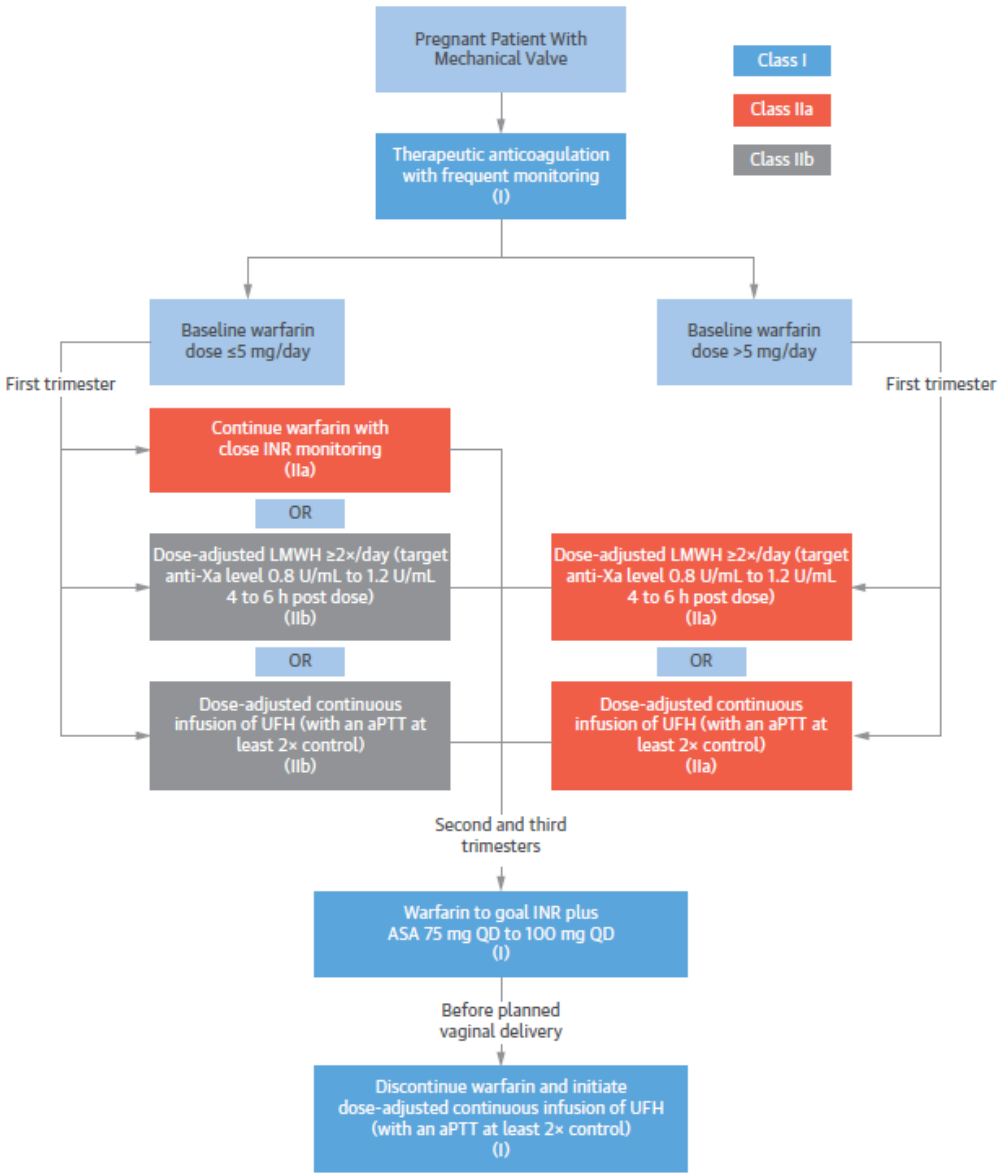
FIGURE 2 Anticoagulation of Pregnant Patients With Mechanical Valves



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

CENTRAL ILLUSTRATION: Cardiovascular Medications in Pregnancy

Arrhythmias

Adenosine	C
Metoprolol/propranolol	C
Digoxin	C F
Lidocaine	B
Verapamil	C
Diltiazem	C
Procainamide	C
Sotalol	B F
Flecainide	C F
Propafenone	C
Amiodarone #	D

may be used if other therapies fail

Heart Failure

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

Anticoagulants/Antiplatelets/Thrombolytics

Anticoagulants	
Warfarin	D
Unfractionated Heparin	C
Enoxaparin	B
Fondaparinux	B
Argatroban	B
Bivalirudin	B
Antiplatelets	
Aspirin (low dose)	N
Clopidogrel	B
Prasugrel	B
Ticagrelor	C
Thrombolytics	
Alteplase	C
Streptokinase	C

Hypertension

Labetalol	C
Nifedipine	C
Alpha-methyldopa (oral)	B
Hydralazine	C
Nitroglycerin	C
Nitroprusside	C
Isosorbide dinitrate	C
Amlodipine	C
Furosemide	C
Hydrochlorothiazide	B
Clonidine	C

Pulmonary Hypertension

Iloprost	C
Epoprostenol	B
Sildenafil	B
Treprostinil	C

Contraindicated in Pregnancy

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

captopril, benazepril and enalapril are considered safe during lactation.
*Variable designation according to specific drug.

Safety in pregnancy | FDA category | Safety in lactation | F: Used also for fetal treatment

- Considered safe
- Limited data/to be used with caution
- Contraindicated
- Conflicting data/unknown

Halpern, D.G. et al. J Am Coll Cardiol. 2019;73(4):457-76.

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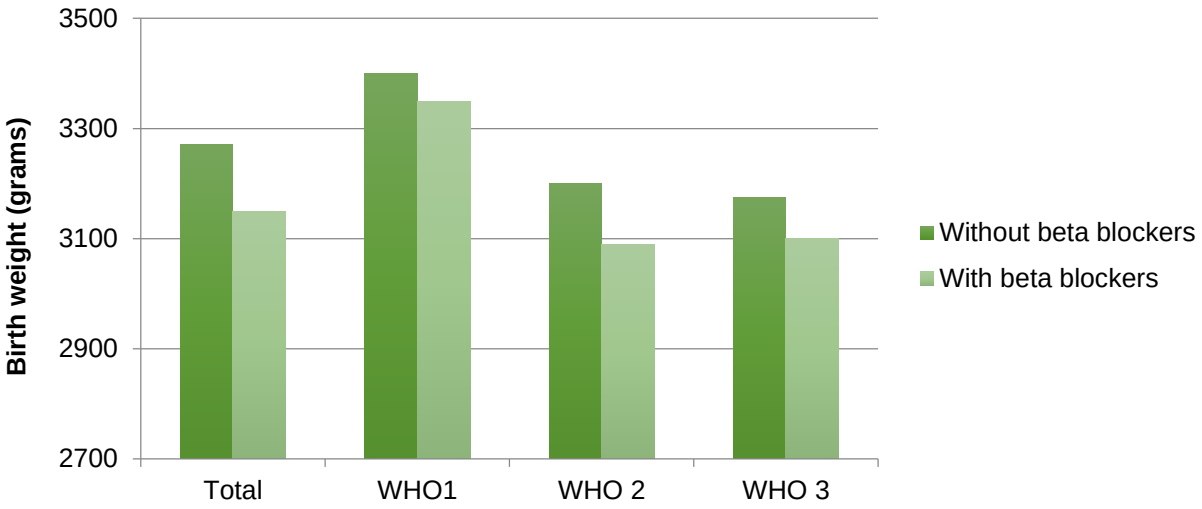
Cardiac medication

during pregnancy, data from the ROPAC

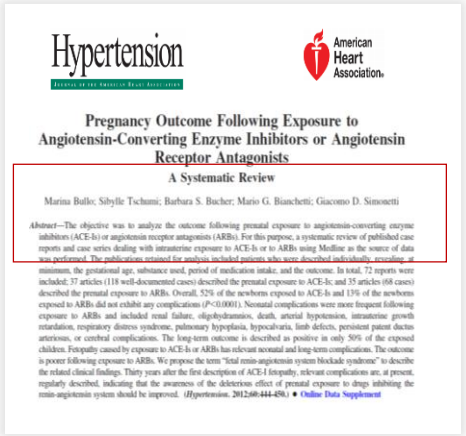


Birth weight in patients with and without beta-blockers per WHO class adjusted for gestational age, smoking, fetal sex, maternal age, diabetes and pre-eclampsia.

Ruys, Maggioni, Johnson, Sliwa, Hall, Roos-Hesselink. International Journal of Cardiology, 2014

Results

48% of the newborns exposed to ACE-Is and 87% of the newborns exposed to ARBs did exhibit any complications (P< 0.0001)



Hypertension

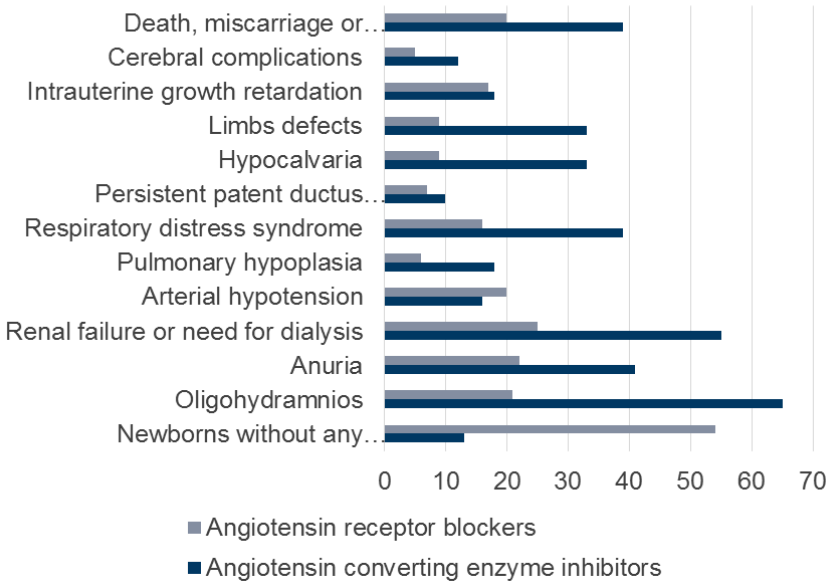
American Heart Association.

Pregnancy Outcome Following Exposure to Angiotensin-Converting Enzyme Inhibitors or Angiotensin Receptor Antagonists

A Systematic Review

Marina Bullo; Sibylle Tschumi; Barbara S. Bucher; Mario G. Bianchetti; Giacomo D. Simonetti

Abstract—The objective was to analyze the outcome following prenatal exposure to angiotensin-converting enzyme inhibitors (ACE-Is) or angiotensin receptor antagonists (ARBs). For this purpose, a systematic review of published case reports and case series dealing with intrauterine exposure to ACE-Is or to ARBs using Medline as the source of data was performed. The publications retained for analysis included patients who were described individually, revealing, at minimum, the gestational age, substance used, period of medication intake, and the outcome. In total, 72 reports were included; 37 articles (118 well-documented cases) described the prenatal exposure to ACE-Is; and 35 articles (68 cases) described the prenatal exposure to ARBs. Overall, 52% of the newborns exposed to ACE-Is and 13% of the newborns exposed to ARBs did not exhibit any complications ($P<0.0001$). Neonatal complications were more frequent following exposure to ARBs and included renal failure, oligohydramnios, death, arterial hypotension, intrauterine growth retardation, respiratory distress syndrome, pulmonary hypoplasia, hypocalvaria, limb defects, persistent patent ductus arteriosus, or cerebral complications. The long-term outcome is described as positive in only 50% of the exposed children. Fetopathy caused by exposure to ACE-Is or ARBs has relevant neonatal and long-term complications. The outcome is poorer following exposure to ARBs. We propose the term "fetal renin-angiotensin system blockade syndrome" to describe the related clinical findings. Thirty years after the first description of ACE-I fetopathy, relevant complications are, at present, regularly described, indicating that the awareness of the deleterious effect of prenatal exposure to drugs inhibiting the renin-angiotensin system should be improved. (*Hypertension*. 2012;60:444-450.) • Online Data Supplement



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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%

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POSITION STATEMENT

Current state of knowledge on aetiology, diagnosis, management, and therapy of peripartum cardiomyopathy: a position statement from the Heart Failure Association of the European Society of Cardiology Working Group on peripartum cardiomyopathy

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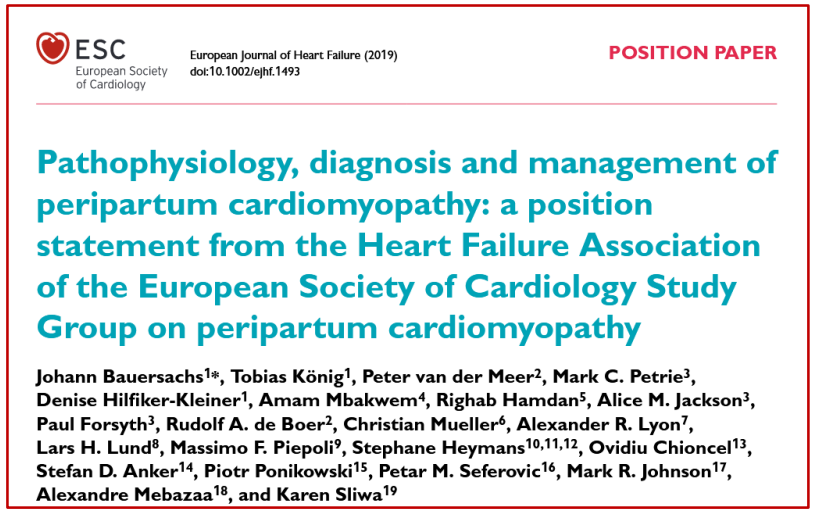

ESC European Society of Cardiology

European Journal of Heart Failure (2019)
doi:10.1002/ejhf.1493

POSITION PAPER

Pathophysiology, diagnosis and management of peripartum cardiomyopathy: a position statement from the Heart Failure Association of the European Society of Cardiology Study Group on peripartum cardiomyopathy

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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.

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- 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.

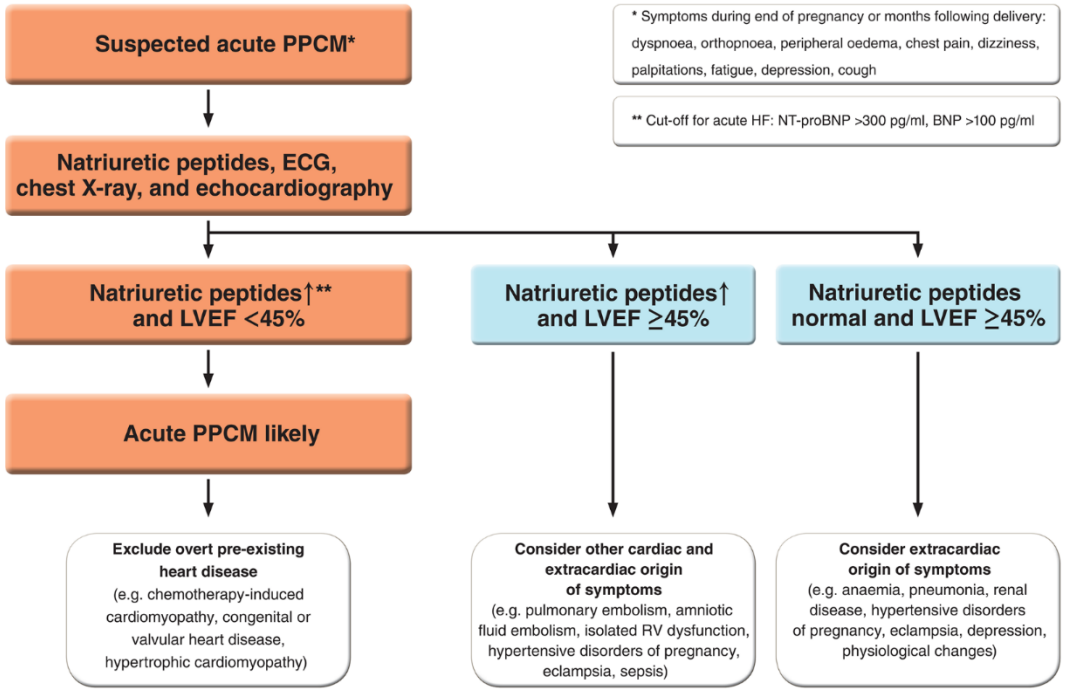

Figure 1: Diagnostic pathway in patients with suspected peripartum cardiomyopathy (PPCM). BNP, B-type natriuretic peptide; ECG, electrocardiogram; HF, heart failure; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; RV, right ventricular.

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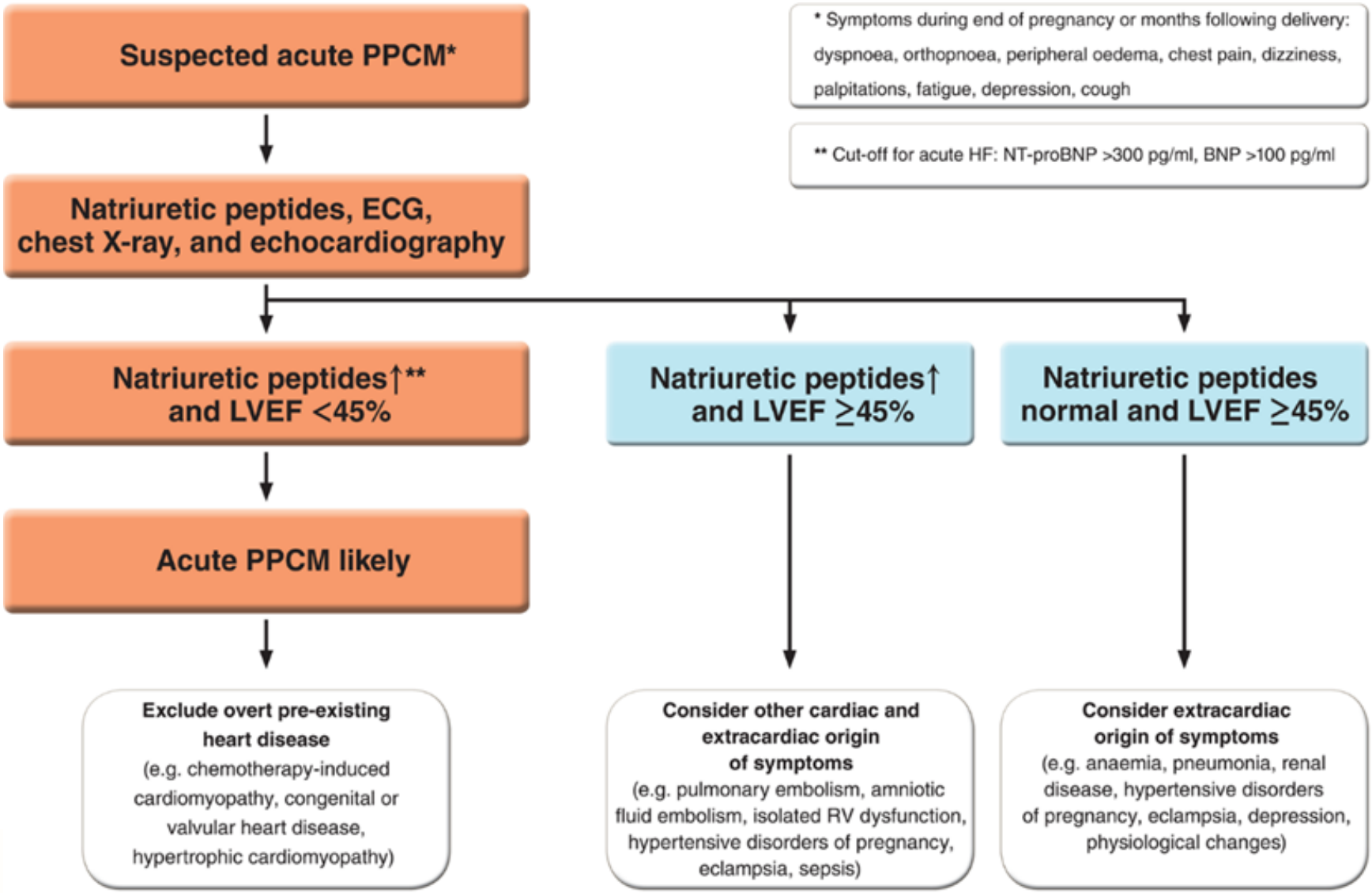
Suspected acute PPCM*
Natriuretic peptides, ECG, chest X-ray, and echocardiography
Natriuretic peptides↑** and LVEF <45%
Natriuretic peptides↑ and LVEF ≥45%
Natriuretic peptides normal and LVEF ≥45%
Acute PPCM likely
Exclude overt pre-existing heart disease (e.g. chemotherapy-induced cardiomyopathy, congenital or valvular heart disease, hypertrophic cardiomyopathy)
Consider other cardiac and extracardiac origin of symptoms (e.g. pulmonary embolism, amniotic fluid embolism, isolated RV dysfunction, hypertensive disorders of pregnancy, eclampsia, sepsis)
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

	Clinical examination	ECG	Natriuretic peptides	Echocardiography	Chest X-ray	Cardiac MRI	CT scan	Coronary angiography
Diagnosis of PPCM	X	X	X	X	X	(X)[b]	(X)[b]	(X)[b]
4-6 weeks after diagnosis	X	X	X	X				
3 months after diagnosis	X	X	X[a]	X				
6 months after diagnosis	X	X	X[a]	X		(X)[b]		
12 months after diagnosis	X	X	X[a]	X				
18 months after diagnosis	X	X	X[a]	X				
Annually for at least 5 years after diagnosis (especially if not fully recovered)	X	X	X[a]	X				

•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.

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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).

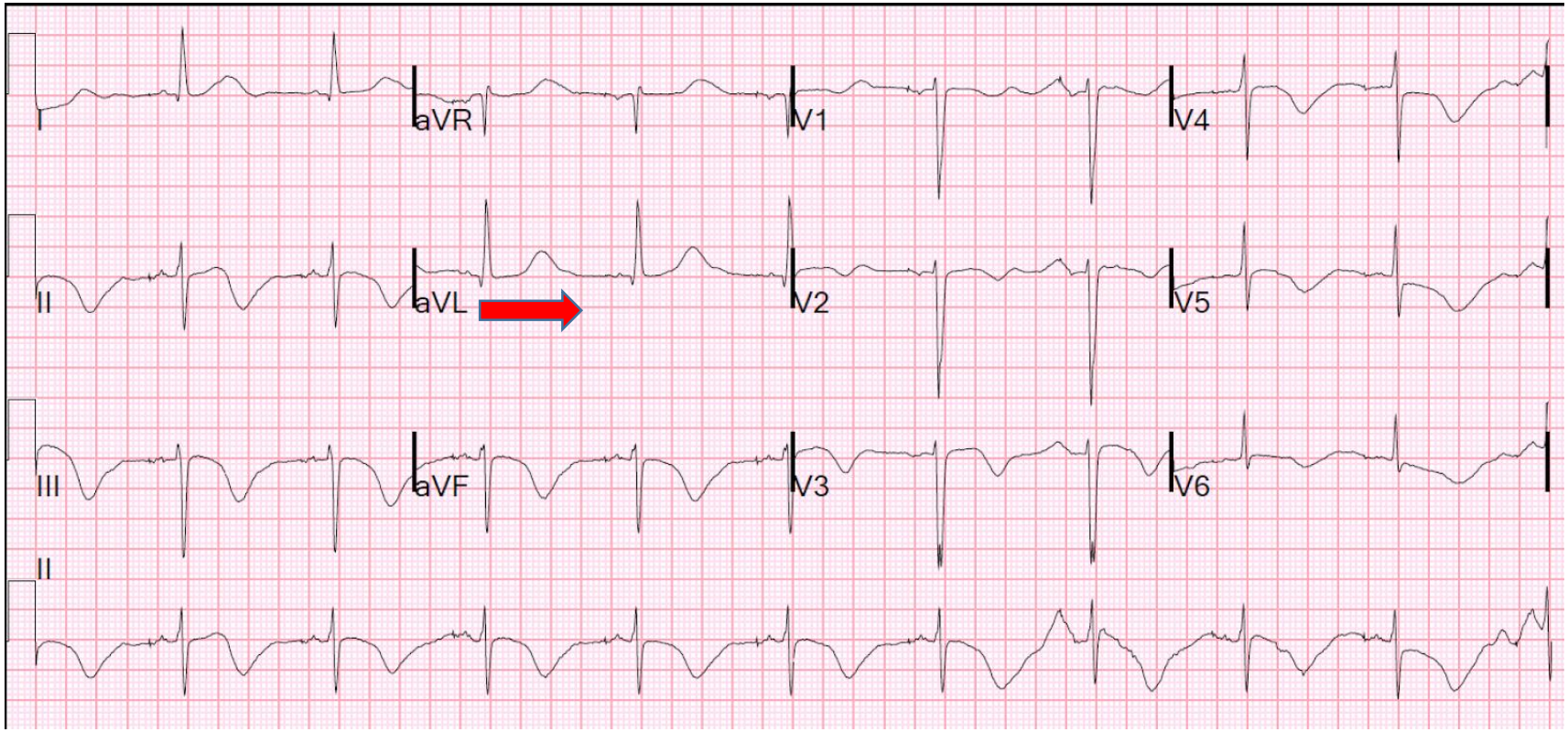

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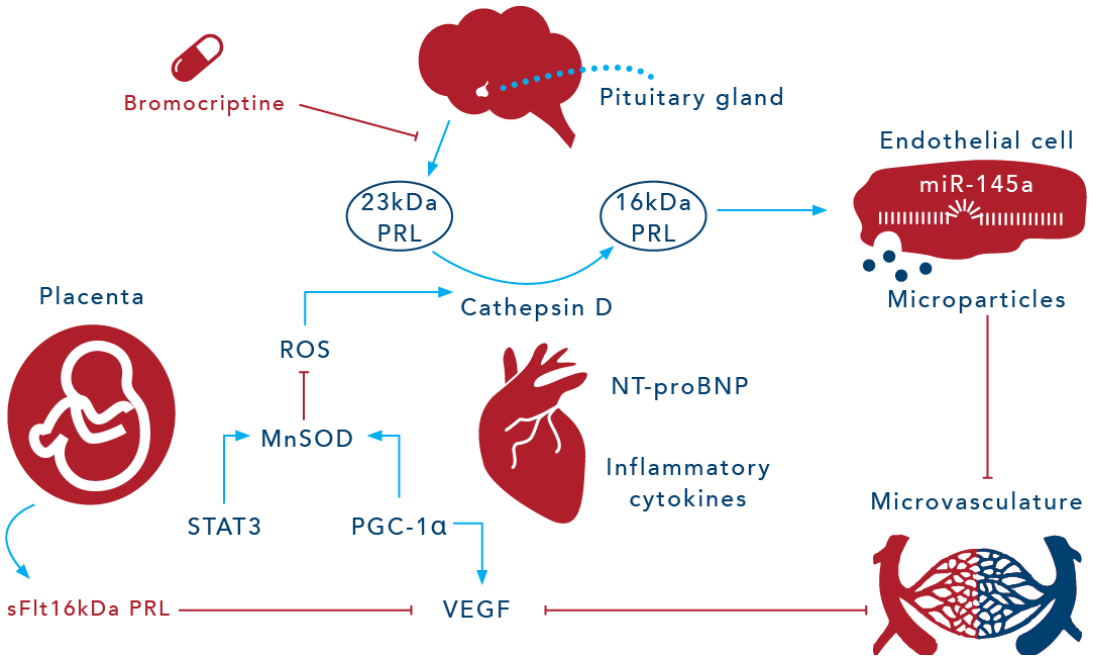
Table: Differential diagnoses of peripartum cardiomyopathy

	History	Onset	Biomarkers	Echocardiography/cardiac MRI	Differentiation from PPCM
PPCM	No known cardiac disease, no HF signs and/or symptoms prior pregnancy	Towards the end of pregnancy and the months following delivery	Elevated natriuretic peptides	Reduced systolic LV function, LVEF < 45%	–
Myocarditis	Prior viral infection (e.g. respiratory)	Acute or subacute onset after viral infection	Elevated troponin, elevated CRP	Normal or reduced systolic LV function, typical myocardial late gadolinium enhancement pattern, pericardial effusion	Cardiac MRI (LE pattern), myocardial biopsy
Pre-existing idiopathic/ familial dilated or acquired cardiomyopathy	HF signs and/or symptoms and/or known heart disease prior pregnancy	During second trimester of pregnancy	Elevated natriuretic peptides	Reduced systolic LV function, RV dysfunction possible, typical myocardial LE pattern (DCM)	History, echocardiography, cardiac MRI (LE pattern)
Takotsubo syndrome	Chest pain, very stressful delivery or emergency due to foetal complications	Acute onset, during delivery or immediately after delivery	Elevated natriuretic peptides	Regional wall motion abnormalities with typical anatomical patterns	History, echocardiography
Pregnancy-associated myocardial infarction	Chest pain, epigastric pain	Acute onset, during pregnancy or immediately after delivery	Elevated troponin	Regional wall motion abnormalities, ischaemic myocardial scar	History, ECG, coronary angiography, cardiac MRI (LE pattern)
Pulmonary embolism	Chest pain, unilateral leg swelling, acute dyspnoea	Acute onset during pregnancy or after delivery	Elevated natriuretic peptides and/or troponin, elevated D-dimer	RV dysfunction, RV dilatation, LV function usually normal	Computed tomography, VQ scan
Amniotic fluid embolism	Chest pain during/immediately after delivery, acute dyspnoea	Acute onset during delivery or immediately after delivery	Elevated natriuretic peptides possible	Reduced RV systolic function, RV dilatation	History, echocardiography
Hypertensive heart disease/severe pre-eclampsia	Pre-existing or new-onset hypertension, proteinuria	During second trimester of pregnancy	Elevated natriuretic peptides	LV hypertrophy, diastolic dysfunction, transient LV dysfunction	History, echocardiography
Hypertrophic cardiomyopathy	Familial predisposition	During second trimester of pregnancy	Elevated natriuretic peptides	LV hypertrophy, typical myocardial late enhancement pattern, LVOTO (HOCM)	History, echocardiography, cardiac MRI (LE pattern)
HIV/AIDS cardiomyopathy	HIV infection, AIDS	During second trimester of pregnancy	Elevated natriuretic peptides	Reduced systolic LV function, LV/RV often not dilated	HIV serology/test
Pre-existing (unknown) congenital heart disease	HF signs and/or symptoms prior pregnancy, known heart disease, prior cardiac surgery	During second trimester of pregnancy	Elevated natriuretic peptides	(Corrected) congenital heart defects, cardiac shunts	History, echocardiography
Pre-existing valvular heart disease	HF signs and/or symptoms prior pregnancy, known heart disease	During second trimester of pregnancy	Elevated natriuretic peptides	Valvular stenosis or regurgitation, prosthetic heart valves	History, echocardiography

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



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.

Sliwa, Lancet 2016; 388: e28–36

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[21] (IC).
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[22] (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[22] (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-naive pregnant PAH patients, initiating treatment should be considered[23] (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)[24,25] (IIbB).
Pregnancy is not recommended in patients with vascular Ehlers–Danlos syndrome[26] (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

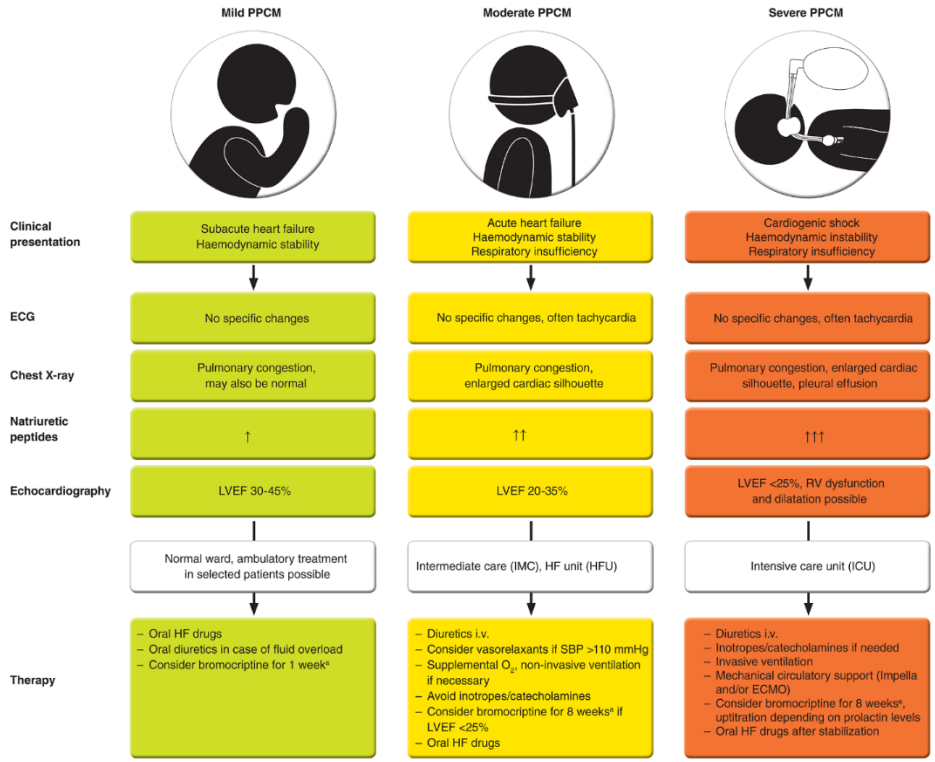
Discussion

What is the diagnosis of our patient?

What investigations should be done?

How should that women be managed?

What pharmacological therapy be started?



FigurePPCM). 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.[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%.**

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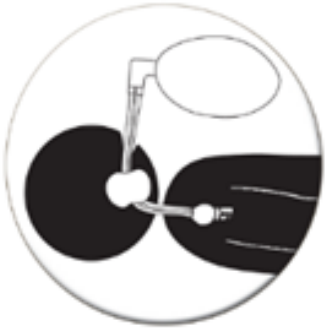
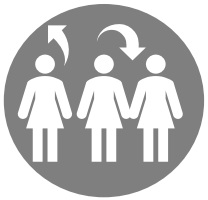


	Mild PPCM	Moderate PPCM	Severe PPCM
Clinical presentation	Subacute heart failure Haemodynamic stability	Acute heart failure Haemodynamic stability Respiratory insufficiency	Cardiogenic shock Haemodynamic instability Respiratory insufficiency
ECG	No specific changes	No specific changes, often tachycardia	No specific changes, often tachycardia
Chest X-ray	Pulmonary congestion, may also be normal	Pulmonary congestion, enlarged cardiac silhouette	Pulmonary congestion, enlarged cardiac silhouette, pleural effusion
Natriuretic peptides	↑	↑↑	↑↑↑
Echocardiography	LVEF 30-45%	LVEF 20-35%	LVEF <25%, RV dysfunction and dilatation possible
	Normal ward, ambulatory treatment in selected patients possible	Intermediate care (IMC), HF unit (HFU)	Intensive care unit (ICU)
Therapy	– Oral HF drugs – Oral diuretics in case of fluid overload – Consider bromocriptine for 1 week[a]	– Diuretics i.v. – Consider vasorelaxants if SBP >110 mmHg – Supplemental O_2, non-invasive ventilation if necessary – Avoid inotropes/catecholamines – Consider bromocriptine for 8 weeks[a] if LVEF <25% – Oral HF drugs	– Diuretics i.v. – Inotropes/catecholamines if needed – Invasive ventilation – Mechanical circulatory support (Impella and/or ECMO) – Consider bromocriptine for 8 weeks[a], uptitration 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