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Review

Pregnancy and delivery in cardiac disease

Titia P.E. Ruys (MD)[a,*], Jérôme Cornette (MD)[b], Jolien W. Roos-Hesselink (MD, PhD)[a]

[a] Department of Cardiology, Erasmus Medical Center, Rotterdam, The Netherlands
[b] Department of Obstetrics & Gynecology, Division of Obstetrics & Prenatal Medicine, Erasmus Medical Center, Rotterdam, The Netherlands

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ABSTRACT

Although its prevalence is relatively low in pregnant women, heart disease is the most important cause of maternal mortality. Problems may arise due to hemodynamic burden and the hypercoagulable state of pregnancy. Heart disease may be congenital or acquired. In developed countries, the former composes the biggest part of women with heart disease. Patients with unrepaired lesions, cyanotic lesions, diminished systemic ventricular function, complex congenital heart disease, left ventricular outflow tract obstruction, pulmonary hypertension, or mechanical valves are at highest risk of developing complications during pregnancy.

All patients with known cardiac disease should preferably be counseled before conception. Pre-pregnancy evaluation should include risk assessment for the mother and fetus, including medication use and information on heredity of the cardiac lesion. Management of pregnancy and delivery should be planned accordingly on individual bases. The types of complications are related to the cardiac diagnosis, with arrhythmias and heart failure being most common. Treatment options should be discussed with the future parents, as they may affect both mother and child. In general, the preferred route of delivery is vaginal. The optimal care for pregnant women with heart disease requires multidisciplinary involvement and is best concentrated in tertiary centers.

Contents

* Corresponding author at: Erasmus Medical Centre Ba 308, P.O. Box 2040, 's-Gravendijkwal 230, 3000 CA Rotterdam, The Netherlands. Tel.: +31 10 703 2432; fax: +31 10 703 5498.
E-mail address: p.ruys@erasmusmc.nl (T.P.E. Ruys).

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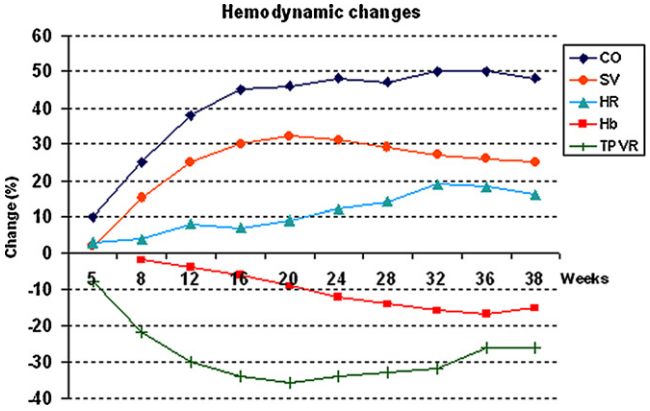

Fig. 1. Hemodynamic changes in pregnancy. CO, cardiac output; SV, stroke volume; HR, heart rate; Hb, hemoglobin; TPVR, total peripheral vascular resistance.

Introduction

Epidemiology

In the developed world many women with congenital heart disease are reaching childbearing age and wish to become pregnant.

While congenital heart disease is more often encountered than acquired disease in pregnant women, it seems associated with a lower risk. Acquired conditions such as aortic dissection, peripartum cardiomyopathy, and acute coronary syndrome (ACS) cause the highest maternal mortality rates [1,2]. Pregnancy increases the risk of having an ACS three- to four-fold [3]. The overall incidence of pregnancy related ACS is reported to be between 2.7 and 6.2 per 100,000 deliveries and this figure is increasing, probably due to changes in lifestyle, higher prevalence of obesity, and older age at pregnancy [3,4]. In the developing world, rheumatic heart disease remains the most common pathology [5].

Physiological changes in normal pregnancy

Major hemodynamic changes take place during pregnancy. Total peripheral vascular resistance (TPVR) is reduced and blood volume and cardiac output are increased around 50% [6]. During labor and delivery, cardiac output is further increased as a result of uterine contractions and maternal effort [6]. After delivery, most changes are rapidly reversed in the first 2 weeks with further normalization toward preconception values after 3–12 months. Fig. 1 shows the hemodynamic changes. However, some structural changes might never completely be reversed.

In order to reduce blood loss around delivery, the production of tissue plasminogen activator (tPA), protein C and S is decreased and tPA inhibitor and factors V, VII, VIII, IX, X, XII and von Willebrand factor are increased, leading to a hypercoagulable state [7–9].

Management of pregnancy in women with heart disease

Pre-pregnancy counseling

Counseling after thorough evaluation should be offered to all women of reproductive age with known cardiac disease. This should preferably be done before conception or alternatively in early pregnancy [5]. Risk for persistent deterioration of heart function may influence the choice whether to become pregnant. Pre-pregnancy evaluation should focus on identifying and quantifying risks for both mother and offspring. An exercise test (with VO2 max measurements) and echocardiogram provide essential information on pre-pregnancy cardiac status and reserve.

Life expectancy and ethical aspects of parenthood should also be discussed during the pre-pregnancy consultation. Genetics and inheritance will be of special interest in some patient groups (congenital heart disease, Marfan syndrome, and hypertrophic cardiomyopathy) [5]. The advantages and disadvantages of medication should be discussed including teratogenicity. If necessary, drug schedules should be adapted. More information on medication in pregnancy can be found in Table 1.

Several risk stratification models have been described over the years. Siu et al. published the CARPREG risk score in 2001 mainly based on women with congenital and valvular heart disease. Significant predictors for adverse maternal and neonatal outcome were prior cardiac events (heart failure, transient ischemic attack, stroke before pregnancy or arrhythmia), baseline New York Heart Association (NYHA) functional class >II or cyanosis, left heart obstruction (mitral valve area <2 cm^2, aortic valve area <1.5 cm^2, peak left ventricular outflow tract gradient >30 mmHg by echocardiography) and reduced systemic ventricular systolic function (ejection fraction <40%) [10]. Khairy et al. found additional predictors for adverse outcome namely a history of smoking and severe pulmonary regurgitation [11]. The ZAHARA investigators showed in a large retrospective cohort of women with congenital heart disease that a history of arrhythmic events or mechanical valve implantation are independent predictors for maternal and neonatal complications [12]. The World Health Organization (WHO) developed a risk score based on cardiac pathology and co-morbidity. WHO class 1 indicates low risk, WHO class 2 indicates an intermediate risk, WHO class 3 indicates high risk, and WHO class 4 indicates a contraindication for pregnancy (Table 2) [13].

Complications during pregnancy

The type of complication depends on the specific cardiac pathology (Table 1). Arrhythmias and heart failure are the most common complications encountered [14].

Heart failure: All patients with heart failure during pregnancy should be admitted for bed rest. Medical treatment includes salt and fluid restriction, diuretics to limit the volume load, and antihypertensive therapy for afterload reduction. Angiotensin-converting enzyme (ACE) inhibitors can induce fetal anuria, pulmonary hypoplasia, and skull deformities especially when used in the second and third trimester. They are, therefore, contraindicated during pregnancy. However, in some specific situations the maternal benefits can outweigh the fetal risks and ACE inhibitors may be used for a short time [5,15].

Arrhythmias: The incidence of arrhythmias may be increased during pregnancy in women with heart disease. When drug therapy is deemed necessary, beta-blockers or digoxin are the preferred choice. The latter can be used in women with atrial fibrillation. Due to the increase in blood volume during pregnancy, higher doses are necessary to reach adequate blood levels. Electrical cardioversion is the treatment of choice for all drug-refractory maternal arrhythmias. It can be performed safely during pregnancy [16].

Bradyarrhythmias are uncommon and usually well tolerated. Pacemaker implantation may be necessary in selected patients whereby radiation should be kept to a minimum [17]. Ectopic beats are often benign and also present in one-third of healthy pregnant women. Management mainly consists of reassurance. Supraventricular tachyarrhythmias are rare [17]. Nakagawa et al. studied 11 patients with new-onset ventricular arrhythmia during pregnancy, 73% of these originated from the right ventricular outflow tract, post-pregnancy the arrhythmia disappeared completely in all patients [18].

Table 1
Medication during pregnancy. Food and drug administration (FDA) classification: *Category A:* Adequate and well-controlled studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of risk in later trimesters). *Category B:* Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women. *Category C:* Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks. *Category D:* There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks. *Category X:* Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.

Medication	FDA	Information
Atenolol	D	Intrauterine growth restriction and premature birth
Other beta-blockers	C	Low birth weight, hypoglycemia, and bradycardia in the fetus
Angiotensin-converting enzyme inhibitors	D	High incidence fetal death and fetotoxic effect: renal failure, renal dysplasia
Amiodarone	D	Thyroid insufficiency
Angiotensin receptor blockers	D	High incidence fetal death and fetal renal failure
Aspirin	B	Low-dose aspirin is safe (large database)
Calcium channel antagonists	C	Diltiazem: an increase in major birth defects has been reported
Clopidogrel	B	The benefits of using clopidogrel in some high-risk pregnancies may outweigh the potential fetal risks
Digoxin	C	No reports of congenital defects, monitor serum levels
Loop diuretics	C	Hypovolemia can lead to reduced uterine perfusion
Low molecular weight heparin and unfractionated heparin	C	Factor Xa should by measured weekly, levels may fluctuate during pregnancy
Nitrates	B	Careful titration is advised to avoid maternal hypotension
Spironolactone	D	Potential anti-androgenic effects on the developing male fetus
Statins	X	Animal studies demonstrated increased skeletal abnormalities, fetal and neonatal mortality.
Thiazide diuretics	B	Hypovolemia can lead to reduced uterine perfusion

Diagnosis in pregnancy

Identifying deterioration of an existing cardiac condition can be a diagnostic challenge as cardiopulmonary signs and symptoms reported during normal pregnancy closely mimic heart disease. In addition, acquired heart diseases often present acutely and catastrophically in women with no known pre-existing disease. Recognition of the acute presentation, immediate diagnostic examination, and appropriate management will improve their chances of survival [15].

Physical examination: In a healthy pregnant woman, normal findings include a mild increase in resting heart rate, a widened pulse pressure, peripheral edema, and a slight elevation of venous pressure. During the later stages of pregnancy there is a physiological fixed splitting of the second heart sound (S2). Systolic murmurs are common, secondary to the increased cardiac output. However, diastolic murmurs are unusual and therefore call for further evaluation [16].

Electrocardiogram: The electrocardiogram changes as a result of the upward shift of the diaphragm caused by the growing uterus. There is left axis deviation and in the third trimester Q waves in lead III and aVF and inverted T waves in leads III, V1, and V2 are seen [17].

Echocardiography: Trans-thoracic (and trans-esophageal) echocardiography is a safe, rapid, and useful diagnostic tool. In a normal pregnancy a significant increase in cardiac output, cardiac index, left ventricular end-diastolic volume, and left ventricular wall thickness is observed [17]. Cardiac ultrasound is indicated in women with symptoms of cardiac disease as well as in women with established heart disease in order to monitor cardiac condition and valvular function [5]. In patients with aortic dilatation, echocardiography should be done at 6–8 weeks intervals throughout the pregnancy until 6 months postpartum [15].

Imaging: Chest X-ray should be performed on indication [19]. Magnetic resonance imaging (MRI) may be useful in complex heart disease and aortic pathology. MRI is considered to be safe from 12 weeks' gestation. Gadolinium contrast is best avoided [20].

Laboratory: For the diagnosis of ACS both creatinine kinase (CK) MB and troponin are used. During labor elevated CK and CK MB can be found due to uterine contractions. These levels normalize during the second day after labor [21]. Troponin I is not elevated in normal pregnancy, as a result troponin I is the recommended laboratory test in pregnancy [22]. However, troponin I serum levels can be elevated in patients with pre-eclampsia or a hypertensive crisis. It is not clear whether this is a sign of cardiac ischemia in these patients. Increased B-type natriuretic peptide levels are found during pregnancy in many pregnant women with heart disease. In the study by Tanous et al. B-type natriuretic peptide levels lower than 100 picograms per milliliter had a negative predictive value of 100% for identifying events during pregnancy. Therefore during pregnancy serial B-type natriuretic peptide levels could be helpful, specifically in excluding suspected adverse cardiac events [23].

Treatment during pregnancy

Medication: Table 2 shows the safety profile of commonly used cardiovascular drugs during pregnancy.

Interventional treatment: An intervention may arise when cardiac function deteriorate during pregnancy or when a cardiac condition is either unknown or underestimated before pregnancy [24]. In emergency situations, interventional procedures are justified. Ultrasound-guidance and abdominal shielding can help to limit fetal radiation exposure to acceptable doses. The uterus receives radiation scattered from the irradiated area, which is more important than the direct exposure (only 2%). The actual risk depends on the dose and stage of development of the fetus. Radiation doses to the fetus higher than 50–100 mGy place the child at risk for growth retardation, malformation, or miscarriage. For low doses to the fetus, the principal risk is radiation-induced cancer (stochastic effects) [19].

Cardiac surgery: Cardiac surgery during pregnancy should only be done if all other treatment modalities (medication and percutaneous intervention) have failed. Intraoperative hypotension and hypothermia, embolic complications, and placental hypoperfusion and preterm labor cause fetal mortality in 14–33% or severe morbidity in another 20% where maternal mortality is not much encountered. Severe maternal illness, total operative time, emergency surgery, necessity of revision, advanced maternal age, and gestational age are all associated with poorer outcome [25].

Fetal heart rate monitoring eventually combined with intermittent uterine and umbilical artery Dopplers reflect placental

Table 2
Different diagnoses with corresponding risks categories and most encountered problems.

Type of heart disease	WHO categories	Most often encountered complications	Other important information
Congenital heart disease (*corrected*)			
Atrial septal defect	1	Arrhythmias (1%)	In uncorrected atrial septal defect higher risk of pre-eclampsia
Ventricular septal defect	1	Premature delivery (12%)	In uncorrected ventricular septal defect higher risk of pre-eclampsia
Atrio-ventricular septum defect	2 or 3	Arrhythmias (10%)/deterioration of atrio-ventricular valve regurgitation (17%)	Recurrence of congenital heart disease in up to 10%
Tetralogy of Fallot	2	Arrhythmias (6%)	Patients with severe pulmonary regurgitation are at risk for progressive right ventricular dilation
Coarctation of the aorta	2 or 3	Hypertensive disorders (11%)	Increased risk of aortic dissection
Transposition of the great arteries (Mustard/Senning)	3	Arrhythmias (22%)/heart failure (11%)	Irreversible ventricular dysfunction in 10%
Fontan operation	3	Arrhythmias (16%)/heart failure (4%)	In case of cyanosis risk for miscarriage
Eisenmengers syndrome	4	Heart failure (21%)/maternal mortality up to 50%	Mainly in post-partum period (first 3 days)
Valvular heart disease			
Mitral stenosis	2 or 3	Heart failure (31%)/arrhythmias (11%)	Mainly in patients with mitral valve < 1.5 cm^2
Aortic stenosis	2 or 3	Heart failure (3–44%)/arrhythmias (6–25%)	Mainly in patients with an aortic valve < 1.5 cm^2
Pulmonary stenosis	1	Right sided heart failure (9%)	Mainly in patients with moderate to severe pulmonary stenosis
Regurgitation lesions	1 or 2	Heart failure (7%)/supra ventricular tachycardia (9%)	Mainly in patients with decreased cardiac function at baseline
Mechanical valves	3	Valvular thrombosis up to 10% maternal mortality up to 4%	Outcome depends on anticoagulation regimen used
Cardiomyopathy			
Peri-partum cardiomyopathy in current pregnancy	2 or 3	Severe heart failure at the end of pregnancy 100%, maternal mortality in 15%	Half of the patients have complete recovery of ventricular function
Peri-partum cardiomyopathy in previous pregnancy without abnormal ventricular function	2 or 3	Recurrence of heart failure (21%)	Ventricular function further decreases in some patients
Peri-partum cardiomyopathy in previous pregnancy with abnormal ventricular function	4	Recurrence of heart failure (44%) maternal mortality (20%)	Ventricular function further decreases in most patients
Dilated cardiomyopathy	2 or 3	Heart failure (25%) arrhythmia's (19%)	Mainly in patients with abnormal ventricular function (left ventricular ejection fraction <45%) at baseline
Hypertrophic obstructive cardiomyopathy	2 or 3	Heart failure (28%)	Mainly in symptomatic patients at baseline, beta-blockers should be considered
Hypertrophic non obstructive cardiomyopathy	2 or 3	Low risk of heart failure	Mainly in symptomatic patients at baseline
Ischemic heart disease			
Before pregnancy	2 or 3	Recurrence risk unknown, heart failure in patient with reduce ventricular function	Increasing prevalence in recent decades
During pregnancy	Not applicable	Maternal mortality (9%)	Electrocardiographic changes and troponin are essential diagnostic tools
Peri-partum	Not applicable	High risk of coronary dissection (34%) Maternal mortality (18%)	Coronary dissection partly due to hormonal changes during the last trimester and hemodynamic burden
Aortic disease			
Marfan	2 or 3	Aortic dissection (1–10%)	High risk in patients with aortic diameter > 45 mm
Bicuspid aortic valve disease	2 or 3	Aortic dissection (<1%)	High risk in patients with aortic diameter > 50 mm
Turner's syndrome	3	Hypertensive disorders (67%)/aortic dissection (5%)	Women with Turner's syndrome are often not fertile
Ehlers-Danlos	3 or 4	Maternal mortality (11.5%)	An increased risk of spontaneous uterine rupture
Pulmonary arterial hypertension	4	Maternal mortality (17–33%)	Mainly in post-partum period (first 3 days)

perfusion and should be used to guide bypass pump flow. However, one should take into account that fetal heart rate variability and movements will probably be depressed as a result of the central anesthetics and hypothermia. External tocolysis and clinical examination might reveal uterine contractions. Due to an increased risk of malformations, surgery is best avoided in the first trimester. In the third trimester, the risks of prematurity should be balanced against the risks of surgery. Therefore European guidelines advise considering delivery before surgery after 28 weeks of gestation [26].

Management of delivery

Delivery team

Timing and mode of delivery should be discussed in advance in a multidisciplinary team consisting of at least an obstetrician, an anesthesiologist, and a cardiologist. The patient's preference should to be taken into account and she should be thoroughly counseled about the delivery plan and potential complications. A written

record should be available at all times for all involved caregivers and should include plans to manage foreseeable complications.

Timing

In asymptomatic women in good condition, spontaneous delivery can be awaited. In women with complex lesions, severe cardiac dysfunction, heart failure, aortic dilatation, Eisenmenger syndrome, or mechanical valve switched to heparin, a planned delivery might be more appropriate. Maternal or fetal condition might warrant a planned delivery before 37 weeks.

Mode of delivery

The mode of delivery mainly depends on obstetric indication and the maternal hemodynamic condition. Vaginal delivery is preferred in women with adequate cardiac output. According to the European guidelines, primary Cesarean section should be considered for the patient on oral anticoagulants (OAC) in pre-term labor, in women with severe heart failure, aortic root diameter >45 mm, and patients with acute or chronic aortic dissection [5,27].

Vaginal delivery

Vaginal delivery is uncomplicated in most women with heart disease. Decreased blood loss, more rapid recovery, absence of abdominal surgery, and decreased thrombogenic risks are the most important benefit over Cesarean section. Adequate pain relief with epidural analgesia can help to attenuate the hemodynamic changes that accompany labor and delivery. It also allows controlled fetal descent to the pelvic floor by suppressing bearing down reflex. As such the need for bearing down effort with accompanying Valsava manoeuver is often reduced. Epidural catheters are contraindicated in women using anticoagulants. Alternatives like intravenous analgesia can be considered. Adequate measures to prevent a sudden fall in peripheral vascular resistance associated with epidural anesthesia should be taken in women with left ventricular outflow tract obstruction [28]. Assisted vaginal delivery (by vacuum or forceps extraction) is recommended when excessive maternal efforts and prolonged labor are contraindicated. Cervical ripening using either prostaglandins or mechanical methods and induction of labor with oxytocine are relatively safe in most women with cardiac disease [29].

Cesarean section

Cesarean delivery annihilates the hemodynamic changes associated with labor. It also often permits more appropriate invasive and non-invasive hemodynamic monitoring and management. However it increases the risk of venous thrombo-embolism, infection, and post-partum hemorrhage. Controlled loco-regional anesthesia is often possible and preferred. However some cases may warrant general anesthesia [30,31].

Post-partum period

Care should be given with intravenous bolus of oxytocine in the third stage of labor, as it might cause a sudden fall in cardiac output. Controlled intravenous infusion might be more appropriate. Also certain intravenous prostaglandins, used to prevent or treat post-partum hemorrhage can cause coronary vasospasms (such as sulprostone).

The volume shifts caused by auto-transfusion the first days after delivery have deleterious effects on patients with diminished left ventricular function. Several days of close monitoring for signs of heart failure is recommended in high-risk women [5]. Prophylactic diuretics and ACE inhibitors may be indicated in high-risk patients with severe systemic ventricular dysfunction. A routine echocardiographic examination post-delivery in high-risk women is advisable, paying careful attention to the aortic root in women with Marfan syndrome or aortic valve disease. The risk of thrombo-embolic complications is further increased post-partum and anticoagulation should be adjusted accordingly [9].

In patients with low risk for heart failure and with normal ventricular function, a short observation period of several hours up to 48 h post-partum might be sufficient. While lactation is possible in most women with heart disease, it might be contraindicated due to medication use, severely decreased effort tolerance, or risk of mastitis and bacteremia in some women. The use of diuretics can complicate the initiation of milk production.

Fetal outcome

Predictors

Neonatal outcome is strongly correlated with maternal outcome. Similar to maternal risk factors, several predictors for neonatal outcome have been described such as baseline NYHA class >II or cyanosis, left heart obstruction, smoking during pregnancy, the use of oral anticoagulants during pregnancy, mechanical valve prosthesis, and multiple gestation. Cardiac surgery causes high fetal mortality during pregnancy (up to 30%) [23].

Monitoring

Genetic counseling and invasive prenatal diagnosis should be offered women carriers of known genetic anomalies (e.g. Marfan syndrome, 22q11 deletions, familial cardiomyopathies, and arrhythmias). A second trimester ultrasound screening for fetal abnormalities with special focus on potential congenital heart defects is indicated in all women with congenital heart disease as the risk for congenital heart disease in the offspring is around 3–5% [5,32]. From 24 weeks' gestation, assessment of fetal growth and well-being should be performed at regular intervals using clinical examination, ultrasound biometry and biophysical profile, uteroplacental and fetal Dopplers, and fetal heart rate monitoring as appropriate [33].

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