Cardiac disease in pregnancy

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Abstract

Cardiac disease in pregnancy remains the leading cause of maternal mortality. In this review article we discuss our approach to caring for pregnant women with cardiac disease, and how the physiological changes of pregnancy can impact pre-existing conditions. This is illustrated by case discussions and practice points. Multi-disciplinary, individualised care is paramount to optimising outcomes for pregnant women with cardiac disease and their babies.

Keywords Cardiac disease; Heart; Pregnancy; Review

Introduction

Cardiac disease affects 1–4% of pregnant women. It remains the leading cause of maternal mortality in the United Kingdom (UK). 11% of maternal deaths recorded in the 2017 Confidential Enquiry (2013–2015 triennia) were attributable to cardiac disease. The 2016 MBRRACE report emphasised the importance of maintaining a low index of clinical suspicion for new cardiac disease in pregnant women, and of referring women with known cardiac disease for pre-pregnancy counselling and multidisciplinary care.

The European Society of Cardiology (ESC) 2018 guidelines for the management of cardiac disease during pregnancy highlights the importance of the multi-disciplinary team in the care of pregnant women, including obstetricians, cardiologists and anaesthetists, with other experts (such as neonatologists and haematologists) providing input depending on the needs of the woman in question. Individualising care, with the woman at the centre of this process and fully involved in the decision making, is key to optimising pregnancy outcome. The overall responsibility for co-ordinating and communicating the pregnancy care plan lies with the consultant obstetrician.

Traditionally, many women with cardiac disease in pregnancy have been offered caesarean birth. However, there is increasing concern about the surgical morbidity this brings, and additional risks posed to future pregnancy, with no evidence of a reduction in cardiovascular complications. For the majority of women, vaginal birth can be safely offered. The ESC 2018 guidelines suggest that caesarean birth should be reserved for women who present in labour while receiving oral anticoagulants, certain aortopathies, acute intractable heart failure, and severe pulmonary hypertension.

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Physiological changes of pregnancy

The physiological changes in the cardiovascular system (Table 1) during pregnancy are profound, and may cause women with cardiac lesions to decompensate. The times of most marked change are the second trimester and the peripartum period. These, along with the hypercoagulable state of pregnancy, must be considered when formulating care plans. The impact of these changes will vary according to the nature of the cardiac disease.

Risk assessment

When planning the care of women with cardiovascular disease in pregnancy, several factors determine the level of risk which a pregnancy poses to the woman's current and future health, and the likelihood of a good pregnancy outcome. Ideally, a risk assessment should be performed by the specialist team prior to conception, to facilitate women making an informed choice about whether to proceed. This can form part of pre-pregnancy counselling, at which point a provisional care plan for the pregnancy can be made, and medication altered as necessary. Important factors to consider in the risk assessment include:

- nature of the cardiovascular condition
- current status (corrected or uncorrected, severity)
- medication
- exercise tolerance
- comorbidities (e.g. BMI, hypertension, diabetes, smoking status)
- obstetric history

The ESC recommend the use of the modified World Health Organisation (mWHO) classification of maternal cardiovascular risk to determine the likelihood of a cardiovascular event during pregnancy, and use this to guide the nature and location of care provision.

Principles of care for women with cardiovascular disease in pregnancy

Maternal considerations:

- How are the physiological changes of pregnancy and birth likely to affect the woman's heart?
- Are peripartum anaesthetic agents or medications safe?
- What contraceptive options are recommended?

Fetal considerations:

- What is the chance of the baby inheriting the same condition?
- Will medication prescribed for the maternal cardiovascular disease affect the fetus?
- How will the maternal condition affect fetal wellbeing?

The scenarios described below illustrate how these principles can be applied in practice.

Cardiovascular physiological changes of pregnancy

	Pregnancy	Intrapartum	Post-partum
Cardiac output	↑by 40%	↑by 15% (1st stage) ↑by 50% (2nd stage)	↑ by 60—80% in the first hour and then ↓over the next 24 weeks
Stroke volume	↑	↑	↓
Heart rate	↑ by 10—20 beats	↑	Returns to pre-pregnancy level over first 2 weeks
Blood pressure	↓first and second trimester ↑third trimester	↑	Falls initially and then increases Day 3—7. Returns to pre-pregnancy level by 6 weeks
Systemic vascular resistance (SVR)	↓	↑	↑by 30% over first 2 weeks above delivery values

Table 1

Case 1: Mechanical mitral valve in pregnancy

A 22-year-old woman was referred to the obstetric cardiac service at 6 weeks in her first pregnancy. She was born with an atrioventricular septal defect and had this surgically corrected as a child. At age 15 she had a mechanical mitral valve replacement. She had been on warfarin ever since this procedure and had a home INR (international normalised ratio) testing kit. She required approximately 9 milligrams (mg) per day to maintain her INR in the recommended range (3—4). She smoked 10 cigarettes per day. She had been converted by her general practitioner (GP) to low molecular weight heparin (LMWH) on having a positive pregnancy test, and had discontinued the warfarin. A recent echocardiogram had shown normal left ventricular function, and good function of the mechanical valve. She was seen for an urgent joint consultation by a consultant obstetrician and haematologist.

Maternal considerations:

- *How are the physiological changes of pregnancy and birth likely to affect the woman's heart?*

In view of the fact that left ventricular function is normal, her heart is likely to cope with the increased cardiac output of pregnancy well. However, the hypercoagulable state poses a significant risk. A valve thrombosis is a potentially life threatening complication which would require urgent cardiothoracic surgery.

In a 2016 United Kingdom Obstetric Surveillance System (UKOSS) study of women undergoing pregnancy with a mechanical prosthetic heart valve, 57 women (9%) died, and a further 41% had significant morbidity. The morbidity and mortality amongst these women included cerebrovascular accident and bleeding complications as a result of anti-coagulation at the time of birth.

It is therefore imperative that these women are referred to a specialist obstetric-cardiology service. The options for anti-coagulation need careful consideration. Warfarin crosses the placenta. In the first trimester, exposure may result in an embryopathy, typically causing limb defects and nasal hypoplasia. This occurs in 0.6—10% of exposed fetuses, and is dose dependent. The risk is low if the daily warfarin dose is less than 5 mg. There is also a higher risk of first trimester miscarriage when compared to LMWH. A fetopathy (ocular and central nervous system abnormalities, intracranial haemorrhage) may also occur, which is independent of the dose of warfarin. However, the risk of maternal thrombotic complications is higher with LMWH than with warfarin. Consideration of all of the relevant risk factors, whilst respecting maternal choice, should be given when deciding which anticoagulation regime to use. In the UKOSS study, the rate of good maternal and fetal outcome was highest (56%) when LMWH was used in the first trimester, followed by warfarin in the second and third trimester. Women should also be given the option of terminating the pregnancy if they feel the risks are too great, and this procedure should be supported with appropriate management of their anticoagulation.

- *Are peripartum anaesthetic agents or medications safe?*

The main concern in relation anaesthesia in this case is the anti-coagulation. Time where the anticoagulation is discontinued around the time of birth should be minimised, and therefore it is likely that an epidural anaesthetic will be contraindicated. A spinal anaesthetic may be considered depending on the time, dose, and type of last anticoagulation agent.

- *What contraceptive options are recommended?*

Oestrogen containing agents should be avoided due to increased thrombotic risk.

Fetal considerations:

- *What is the chance of the baby inheriting the same condition?*

The overall incidence of congenital heart defects is approximately 8 per 1000 births. When one parent is affected, the risk of having an affected child is approximately 4%. The mechanism of inheritance is not fully understood. A fetal echocardiogram is indicated at 22—24 weeks' gestation to screen for a congenital heart defect in the baby.

- *Will medication prescribed for the maternal cardiovascular disease affect the fetus?*

As described above, warfarin can cross the placenta and cause embryopathy and fetopathy. Due to immaturity of the fetal liver, the baby's INR is likely to be several fold higher than the mothers at any given warfarin dose. Vaginal birth while the mother is anticoagulated with warfarin is contraindicated due to the risk of intracranial haemorrhage.

- *How will the maternal condition affect fetal wellbeing?*

Women with prosthetic heart valves have been shown to have lower birth weight babies than matched controls without cardiovascular disease. If a woman should suffer a valve thrombosis and cardiogenic shock, there is a higher chance of adverse fetal outcome.

A detailed plan of care for pregnancy and birth was constructed, involving a cardiologist, obstetrician, haematologist, obstetric anaesthetist, paediatric haematologist, neonatologist, the woman and her partner. A plan was made to use LMWH for the first trimester, then convert back to warfarin. Anti- Xa levels were used to ensure adequate anti-coagulation on

LMWH, then INR testing whilst on warfarin. Regular scans were performed by a fetal medicine specialist to assess fetal growth and look for evidence of intracranial haemorrhage. At 35 weeks, she was converted back to LMWH to allow the baby's INR time to normalise prior to birth. Induction of labour was scheduled for 39 weeks. On admission, LMWH was discontinued and intravenous (IV) unfractionated heparin commenced. The infusion was switched off when active labour was confirmed, and recommenced 4 hours post birth. A spontaneous vaginal birth of a healthy male infant ensued and neither had any bleeding complications. Warfarin was recommenced 3 days post birth.

Case 2: Long QT syndrome (LQTS) in pregnancy

A 28-year-old woman who had a known diagnosis of long QT syndrome (type 2) attended for her first clinic appointment at the obstetric cardiac clinic when she was 12 weeks into her first pregnancy. She had been diagnosed with long QT syndrome after her sister died suddenly. She herself had suffered a cardiac arrest 3 years prior to her pregnancy, and subsequently had an implantable cardioverter defibrillator (ICD) fitted. She was under regular cardiology review and taking propanolol 80 mg once a day. She had no other comorbidities, a BMI of 22 and had no restriction to her exercise tolerance.

Maternal considerations:

- *How are the physiological changes of pregnancy and birth likely to affect the woman's heart?*

Episodes of irregular rhythm, potentially resulting in ventricular fibrillation, may be triggered by exercise or stress, as a result of adrenergic stimulation affecting calcium channels in the myocytes. The beta-blocker treatment (propanolol) aims to protect against this. It is imperative that this is continued in the peripartum period, where adrenergic response to pain in labour is most likely.

- *Are peripartum anaesthetic agents or medications safe?*

There are several drugs which may prolong the QT interval and therefore should be avoided in people with long QT syndrome (see www.crediblemeds.org for an up-to-date list). Notably, this includes Syntocinon. Consideration may be given to using these medications in individuals with low risk LQTS, however in this woman they should be avoided.

- *What contraceptive options are recommended?*

There are no restrictions on contraceptive options in women with LQTS.

Fetal considerations:

- *What is the chance of the baby inheriting the same condition?*

LQTS has an autosomal dominant inheritance. This means that with one affected parent, the chance of the baby inheriting the condition is 50%. This woman was aware of the inheritance risk, due to prior genetic counselling, and had opted for pre-implantation genetic diagnosis (PIGD) and in-vitro fertilisation (IVF). She therefore knew that her baby was unaffected. If this had not been the case, genetic counselling and invasive prenatal testing (amniocentesis or chorionic villus sampling) should be offered.

- *Will medication prescribed for the maternal cardiovascular disease affect the fetus?*

Maternal beta-blocker therapy increases the risk of a baby being small for gestational age when compared to other pregnant women. There is also a small risk of neonatal hypoglycaemia.

- *How will the maternal condition affect fetal wellbeing?*

Provided the woman does not undergo a cardiovascular event, there should not be any adverse effects on fetal wellbeing directly relating to the maternal LQTS. If a cardiac arrest should occur, then there is a risk of hypoxia and death to both mother and baby. The ICD aims to reverse a dangerous arrhythmia before cardiac arrest occurs, however avoiding such an arrhythmia occurring is preferable.

There are different types of long QT syndrome, and considering the type and previous cardiac events is essential when planning pregnancy and peripartum care.

In this woman, fetal growth scans initially revealed an estimated weight on the 90th centile. A vaginal birth was preferred, and a detailed birth plan made in conjunction with the woman and the obstetric cardiac multi-disciplinary team (obstetricians, obstetric anaesthetist, cardiologist). The use of Syntocinon was to be avoided, as oxytocin has been shown to prolong the QT interval. If an induction of labour was required, then this would be using prostaglandin and artificial rupture of membranes (ARM), with recourse to a caesarean birth if this was unsuccessful. Ergometrine was prescribed for active management of the third stage. Should emergency surgery be required, diathermy should be avoided, as this may spuriously trigger her ICD to deliver a defibrillator shock. If time allows, cardiac technicians can be called to turn off the device for surgery, and restart if afterwards. Placing a magnet over the device whilst in theatre is an alternative to temporarily disable it, if the use of diathermy was unavoidable.

The woman presented at 39 weeks with reduced fetal movements. The cardiotocograph (CTG) was classified as suspicious, and labour was induced by ARM. She progressed quickly to full dilatation, when she had an assisted birth by Ventouse due to pathological CTG. She and her baby were well following this.

Case 3: Marfan syndrome in pregnancy

A 40-year-old woman with Marfan syndrome was seen at 20 weeks' gestation in her 4th pregnancy. She was para 3, having previously had two vaginal births and most recently a caesarean birth (2 years ago). Her most recent echocardiogram was in the latter stages of her previous pregnancy, at which point her aortic root diameter was 40 mm. Her booking blood pressure was 139/85 mmHg. She had a family history of aortic dissection, affecting her mother and uncle.

Maternal considerations:

- *How are the physiological changes of pregnancy and birth likely to affect the woman's heart?*

The haemodynamic and hormonal changes of pregnancy predispose women with Marfan Syndrome to aortic dissection, which has a high mortality rate. 50% occur in the third trimester and 33% postpartum. The overall risk for a woman with Marfan syndrome having aortic dissection in relation to pregnancy is 3%. The highest risk is in women with an aortic diameter >45 mm, but the risk is less than 1% if the diameter is <40 mm. The family history of aortic dissection and borderline last known aortic root measurement increase the

risk of a pregnancy associated dissection for this woman. An urgent echocardiogram is indicated, to determine if there has been progressive dilatation since her previous imaging. Progressive aortic dilatation, coupled with the family history of dissection, would be an indication to recommend caesarean birth. If the aortic diameter is greater than 45 mm, consideration should be given to aortic root replacement during pregnancy. Caesarean birth should be recommended for this woman if the aortic dimension has increased.

The woman should be counselled about the risk of dissection and advised to be vigilant for chest pain. Should this occur she should seek urgent medical advice. In our unit, she was advised to contact the maternity department given the co-location of cardiothoracic services on our site.

Her booking blood pressure was borderline. Strict blood pressure control is recommended in women with Marfan syndrome, with recourse to beta-blocker therapy in the first instance if hypertension occurs. ESC guidelines recommend that beta-blockers should be considered through pregnancy in women with aortopathies, however there is no evidence that routine treatment with beta blockers, in the absence of hypertension, reduces the risk of dissection.

- *Are peripartum anaesthetic agents or medications safe?*

Care should be taken to avoid rapid changes in blood pressure, which may increase the risk of aortic dissection. Ergometrine should be avoided in this case. If a vaginal birth is planned, an epidural would be recommended to reduce cardiovascular response to pain.

- *What contraceptive options are recommended?*

Oestrogen containing contraception should be avoided, due to the cardiovascular effects, which may increase the risk of aortic dissection.

Fetal considerations:

- *What is the chance of the baby inheriting the same condition?*

Marfan syndrome follows and autosomal dominant pattern of inheritance, so the risk for the baby of inheriting the condition with one affected parent, is 50%. However, the phenotype is not usually apparent until later life.

- *Will medication prescribed for the maternal cardiovascular disease affect the fetus?*

If beta-blockers are used for control of hypertension, they are associated with fetal growth restriction and neonatal hypoglycaemia.

- *How will the maternal condition affect fetal wellbeing?*

If the woman remains well, without medication, there should be no other effects on the fetus.

Case 4: Peripartum cardiomyopathy

A 34-year-old Afro-Caribbean woman with a BMI of 35 presented in her first pregnancy at 32 weeks with headache. On admission, she was also found to be hypertensive with significant proteinuria and a diagnosis of moderate preeclampsia was made. She was started on labetalol 200 mg three times daily, which controlled her blood pressure. Steroids were given for fetal lung maturation. Whilst an inpatient, she complained of worsening breathlessness, associated with orthopnoea and paroxysmal nocturnal dyspnoea. She became tachycardic and tachypnoeic. There was no associated chest pain. A chest X-ray revealed cardiomegaly and pulmonary oedema. An echocardiogram showed that she had a moderately dilated left ventricle with severely impaired systolic function (LVEF < 35 %), A diagnosis of pre-eclampsia with superimposed peripartum cardiomyopathy was made. She was reviewed by the cardiologists and commenced on furosemide intravenously. Her pulmonary oedema improved, observed clinically by reduction in her symptoms of breathlessness and normalising of her pulse and respiratory rate. She had a category 3 caesarean birth at 33 weeks in view of the above diagnosis. She was advised against breastfeeding and bromocriptine was initiated immediately. She remained haemodynamically stable during the procedure and in the immediate postpartum period. She was discharged home on day 5 on bisoprolol (cardioselective beta-blocker); perindopril, (an ACE inhibitor); oral furosemide and low molecular heparin. The bromocriptine was discontinued after 1 week. She was scheduled for review in a cardiology clinic at 2 weeks postnatal.

Maternal considerations:

- *How are the physiological changes of pregnancy and birth likely to affect the woman's heart?*

Pre-eclampsia is a risk factor for developing peripartum cardiomyopathy. Continuing the pregnancy further would pose further risk of complications from pre-eclampsia and a risk of cardiogenic shock. A vaginal birth with an epidural could be considered in women who are cardiovascularly stable, but at this gestation a caesarean birth is recommended. This woman is vulnerable to cardiac decompensation with recurrence of pulmonary oedema due to circulatory fluid shift at the time of birth. Bromocriptine to stop lactation can reduce the high metabolic demand and speed recovery of heart failure.

- *Are peripartum anaesthetic agents or medications safe?*

Due to the vulnerability to pulmonary oedema described above, the priority for peripartum care is to maintain careful fluid balance, and maintain cardiovascular stability as far as possible. Ergometrine should be avoided. Syntocinon has also been associated with tachycardia and hypotension. However, the cardiovascular effects are less pronounced than those of ergometrine, and avoidance of uterotonics may result in a postpartum haemorrhage, causing more pronounced fluid shift and cardiovascular changes. There is evidence that the use of Syntocinon at standard doses does not increase the risk of a cardiovascular event in women with cardiac disease. Giving Syntocinon by *slow* intravenous injection is a compromise in women at high risk, and less likely to provoke a cardiovascular response.

- *What contraceptive options are recommended?*

Oestrogen containing methods should be avoided. A long acting reversible contraceptive should be highly recommended, as a further pregnancy while the left ventricular function is compromised would increase the mortality risk.

Fetal considerations:

- *What is the chance of the baby inheriting the same condition?*

This is an acquired condition, therefore the baby is not at risk of developing it.

- *Will medication prescribed for the maternal cardiovascular disease affect the fetus?*

Diuretics should only be given if there is pulmonary oedema, as it can affect the placental blood flow. Beta-blockers can increase the chance of the baby being small for gestational age. Angiotensin converting enzyme (ACE) inhibitors should be avoided, especially in the second and third trimester, due to a risk of fetopathy (oligohydramnios, renal tubular dysgenesis, neonatal anuria, hypocalvaria, pulmonary hypoplasia, persistent patent ductus arteriosus, mild to severe intrauterine growth retardation, and fetal or neonatal death).

- *How will the maternal condition affect fetal wellbeing?*

Cardiac failure in the woman can result in acute fetal compromise. Assessment of fetal wellbeing through ultrasound biometry, liquor volume and Doppler studies should be performed. Regular cardiotocography should be performed while the woman's condition is unstable.

Peripartum cardiomyopathy (PPCM) is a rare but potentially life-threatening idiopathic cardiomyopathy that presents with heart failure secondary to left ventricular systolic dysfunction towards the end of pregnancy or in the months following delivery, in the absence of any other cause of heart failure. PPCM is a diagnosis of exclusion. Although the left ventricle may not be dilated, the ejection fraction is nearly always reduced below 45% and/or there is fractional shortening <30% on echocardiogram. There is a wide geographic variation in the incidence of the disease, ranging from 1 in 500 live births in Haiti to 1 in 4000 live births in the United States, thought to be related to socioeconomic and genetic factors. Identified risk factors for PPCM include advanced maternal age, multiparity, African-Caribbean race, multiple pregnancy and hypertensive disorders (pre-existing, gestational hypertension or preeclampsia).

Conclusion

The management of cardiac disease in pregnancy should take a multi-disciplinary approach, and be individualised according to the needs of the woman. Many cardiac conditions are well tolerated (for example a small ventriculoseptal defect) and these women may safely opt for a birth at home or in a midwifery led unit. Others, such as those described above, should be managed in specialist centres with co-located cardiology and obstetric services. In all cases the woman should be fully involved in decisions about her care, and her preferences taken into consideration. ◆

FURTHER READING

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Practice Points

- Care should be multi-disciplinary for women during pregnancy with cardiac disease, with early referral to tertiary units
- Consider what impact the physiological changes of pregnancy will have on the cardiac condition itself and make a plan of care to monitor for these and respond appropriately
- Consider what impact the condition will have on the pregnancy, with particular emphasis on the treatments used for the cardiac condition
- Make a careful plan for labour and delivery, and the postnatal period.
- Be aware of the risks of the fetus inheriting a cardiac condition and offer prenatal screening and testing where appropriate. Inform the paediatricians of this risk, and make a postnatal plan for the baby