

## PREGNANCY IN CONGENITAL HEART DISEASE

# Pregnancy in women with congenital heart disease

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## ABSTRACT

**Due to the enormous improvements in the treatment of children with congenital heart disease, an increasing number of patients reach adulthood nowadays. To achieve the aim of excellent care concerning pregnancy in this patient population, a pro-active discussion of pregnancy with all women in this patient population is essential. Several risk stratification models have been developed in order to identify high risk pregnancies and better inform patients about these risks. Counselling and dedicated care are needed to optimise both maternal and fetal outcomes. Better access to health care systems contributes to further improvements in mortality and morbidity. Furthermore a well-developed, multidisciplinary plan for each individual patient concerning pregnancy, delivery and follow-up is essential.** SAHeart 2013;10:616-624

## BACKGROUND

Pregnancy is a challenge to the cardiovascular system even in healthy women. There are significant changes in circulating volume, arterial resistance, heart rate and structural changes in both the heart and great vessels. In structural heart disease, the capacity of the heart to adapt may be insufficient to cope, leading to a higher risk of complications such as arrhythmias or heart failure. Patients with compromised ventricular function, severe valve disease, pulmonary hypertension or cyanosis are especially at risk. The risk of aortic dissection is also elevated during pregnancy due to changes in hormonal status in addition to the haemodynamic changes. Furthermore there is an increased risk of bleeding and thrombosis. Pregnancy may also have an irreversible adverse effect on cardiac function in patients with congenital heart disease. Finally, mothers diagnosed with a congenital heart defect have an elevated risk of having a child with a congenital defect, dependent on the specific diagnosis. The influence of pregnancy on heart disease and vice versa has consequences for the outcome of mother and child.

Cardiovascular disease is the leading cause of mortality in pregnant women in developed countries, whereas in Sub-Saharan countries the obstetric complications, such as hemorrhage and sepsis lead more often to maternal mortality. Heart disease is, however, the main non-obstetric cause of death in developing countries.<sup>(1)</sup>

There is a difference in type and severity of cardiac diseases in pregnant women in African countries compared with those in West-European countries. The most important underlying pathology in

western Europe is congenital heart disease (CHD) whereas in African nations it is rheumatic valvular disease.<sup>(2)</sup> Due to advances in medical care and improvement of surgical facilities, children with congenital heart disease now have an excellent survival rate, with over 90% of children reaching adult age. Consequently the number of women with repaired congenital heart disease contemplating pregnancy is increasing. An on-going worldwide registry demonstrated two-thirds of the structural heart disease in pregnant women consists of congenital heart disease.<sup>(3)</sup>

There is a lack of data concerning exact cardiovascular maternal mortality in South Africa. Overall maternal mortality in 2010 in South Africa was 300 women per 100 000 live births versus less than 20 per 100 000 in European countries. However, this rate of mortality shows a clear decline over the past two decades, probably mainly due to a better accessibility of health care systems.<sup>(4)</sup>

With better access to health care, an accurate approximation of the increasing numbers of women with adult congenital heart disease in child-bearing age will become available.

## PRE-CONCEPTION COUNSELLING

As pregnancy causes a haemodynamic burden, women known with congenital heart disease should be appropriately informed and advised, preferably before conception, thus at young age. The aim of pre-pregnancy counselling is to empower women to make informed choices about their plans to raise a family and to attempt to optimise the maternal condition pre-pregnancy with elective

intervention carried out if necessary. Depending on their underlying condition, clear and extensive information should be provided and assessment of risks should be carried out.

When a patient presents contemplating pregnancy, pre-pregnancy analysis of the current situation is mandatory. This usually involves a detailed overview of the history with diagnosis and past-interventions, a new echocardiographic examination to measure the ventricular function and residual lesions and also an exercise test to assess the clinical condition. In some cases an MRI or CT scan is required, especially when the aorta may be dilated. After careful assessment of the current situation, several issues have to be discussed with the future parents: firstly, the risk for the mother to developing complications including the possible irreversible effect of pregnancy or even not surviving the pregnancy. Secondly, medication use of the mother has to be discussed, as some medication may be harmful for the fetus. Possible alternatives can be discussed. Or, for instance in the case of ACE-inhibitor use for diminished ventricular function, stopping the medication with new echo and

exercise testing to assess the clinical condition and ventricular function after 3 months may be appropriate. Also the risk of miscarriage and fetal problems should be extensively explained to the future parents. Finally, the life expectancy of the mother should be discussed.

### Risk stratification

It is important to stratify risk by using the tool conducted by the World Health Organisation (WHO). It has been shown that this risk stratification has the best predictive power of the current available risk models (Table 1). There is a low incidence of events in women in WHO I, while patients classified as WHO IV (for instance pulmonary arterial hypertension) have a very high risk and indeed should be advised against pregnancy. In WHO III frequent follow-up should be carried out during pregnancy.<sup>(5)</sup>

Apart from the WHO classification, several other risk scores have been developed. Table 2<sup>(6)</sup> shows the additional predictors of maternal cardiovascular events. We listed only the unique risk

**TABLE 1:** Modified WHO classification of maternal cardiovascular risk: Disease specific.<sup>(5)</sup>

Risk class	Type of congenital heart disease	Risk of pregnancy
WHO I	Successfully repaired simple lesions (i.e. ASD, VSD, PDA)	No detectable increased risk of maternal mortality and no/mild increase in morbidity.
	Mild pulmonary stenosis	
	Mild mitral valve prolapse	
	Small patent ductus arteriosus	
WHO II	Unrepaired ASD or VSD	Small increased risk of maternal mortality or moderate increase in morbidity.
	Repaired tetralogy of Fallot	
WHO II-III	Mild left ventricular dysfunction	↓ Significantly increased risk of maternal mortality or severe morbidity.
	Valve disease (not considered WHO I or IV, and non-mechanical)	
	Marfan, without aortic dilatation	
	Bicuspid aortic valve, with dilated aorta <45mm	
	Repaired aortic coarctation	
WHO III	Mechanical valves	Significantly increased risk of maternal mortality or severe morbidity.
	Systemic right ventricle	
	Fontan circulation	
	Marfan: Aortic dilatation 40-45mm	
	Bicuspid aortic valve: Aortic dilatation 45-50mm	
	Other complex congenital heart disease	
WHO IV	Pulmonary arterial hypertension	Extremely high risk of maternal mortality or severe morbidity; pregnancy contraindicated.
	Severe left (systemic) ventricular dysfunction (LVEF <30%, NYHA III-IV)	
	Severe mitral or symptomatic aortic stenosis	
	Marfan: aortic dilatation >45mm	
	Bicuspid aortic valve: Aortic dilatation >50mm	
	Severe aortic coarctation	

WHO = World Health Organization. ASD = Atrial Septal Defect. VSD = Ventricular Septal Defect. PDA = Patent Ductus Arteriosus.

**TABLE 2:** Predictors of maternal cardiovascular event during pregnancy.

Prediction model	Predictor
CARPREG	Prior cardiac event
	NYHA III or IV, cyanosis
	Left heart obstruction
	LVEF <30%
ZAHARA	Cardiac medication
	Atrioventricular valve regurgitation
	Mechanical valve prosthesis
	Cyanotic heart disease
<b>Additional</b>	
Khairy	Right/subpulmonary ventricular dysfunction or severe pulmonary regurgitation
	Smoking history
Song	Right ventricular dilatation
	Pulmonary arterial hypertension
Tanous	Anticoagulation
	BNP >100pg/ml

Modified from Pieper<sup>(4)</sup>  
 NYHA = New York Heart Association. LVEF = Left Ventricular Ejection Fraction.  
 BNP = B-type Natriuretic Peptide.

factors, as some overlap was seen between the studies. The first prediction model developed was composed by the CARPREG investigators<sup>(7)</sup> with validation carried out on a prospective cohort with mainly congenital heart disease.<sup>(8)</sup>

Validation of the CARPREG score by Khairy, et al., resulted in some additional predictors.<sup>(9)</sup> However, the CARPREG score might overestimate the maternal cardiac risks. Adding more predictive factors, conducted by the ZAHARA group approximates a more accurate estimation of risk.<sup>(10)</sup> For more details on the specific prediction rules, we would like to refer to the original articles.<sup>(7,9-12)</sup>

**Subfertility**

Some results have been published on subfertility in women with congenital heart disease (for instance with a Fontan circulation). This might be caused by the hypoxemia before the interventions at neonatal and infant age, resulting in diminished function of the ovaries.<sup>(13,14)</sup> In case of suspicion of subfertility, a patient should be referred to a specialist with expertise in this field. However, fertility treatment should be embarked upon with caution, since ovarian hyperstimulation may be life-threatening to women with heart disease, and multiple pregnancies poorly tolerated.

**Psychological impact**

Alongside the physical topics discussed in this article, one should be aware of the psychological burden as well, with the combina-

tion of having a preexistent congenital heart disease and the worry of potential complications of a pregnancy. There needs to be awareness of the comprehensive effect on mental status. A thorough conversation with these women should be part of pre-conception counselling.

**PREGNANCY: OUTCOME OF PATIENTS WITH SPECIFIC LESIONS**

In a large registry of pregnant women with structural heart disease, of which 66% had CHD, maternal mortality was notably higher than expected (0.5% in patients with congenital heart disease versus 0.007% in the normal population). Moreover, 20% of patients with CHD are admitted to the hospital during pregnancy, compared to 2% in the normal population. Overall, in the CHD population, 8% needs treatment for symptomatic heart failure during pregnancy, while supraventricular arrhythmias were found in 0.7% and ventricular arrhythmias in 1.6% of patients. Frequency of obstetric complications is similar in those with congenital heart disease compared to the normal population, although caesarean section rates were higher. Fetal outcome (Apgar score, preterm births, fetal and neonatal death, as well as birth weight) is slightly worse in patients with congenital heart disease compared to the normal population.<sup>(3)</sup>

**ASD, VSD and PDA**

Septal defects are classified as WHO I, in the case of a small or corrected defect, with little additive risks compared to pregnancy in healthy women. However, patients with a large shunt are at risk of developing heart failure and paradoxical emboli. Patients with a very large shunt complicated by the Eisenmenger syndrome will be discussed elsewhere in this article.

In women with unrepaired atrial septal defects (ASD) more neonatal events occur than in the normal population. Pre-eclampsia, small-for-gestational-age and fetal mortality are more frequently encountered in this group of patients. Additionally, there is contradictory evidence on the need to repair an ASD before pregnancy. It is thought that they have an elevated risk of being affected by a paradoxical thrombo-embolic event, especially during pregnancy because of the presence of a hypercoagulable state and pressure of the fetus on the vena cava inferior causing stasis. The latest European guidelines only suggest providing prevention through compression stockings and limited supine position and immobilisation. A catheter device closure or surgical intervention needs to be considered pre-pregnancy if an ASD is of haemo-

dynamic importance, as the haemodynamic burden of pregnancy may worsen the situation with increasing shunt and the risk of heart failure.<sup>(15)</sup>

A cohort of patients with an isolated ventricular septal defect (VSD) reported in literature, showed a higher frequency of pre-eclampsia, particularly in patients with an unrepaired VSD, while patients with a repaired VSD tended to have more premature deliveries and neonates who were small-for-gestational-age. However, maternal cardiovascular events are rarely seen.<sup>(16)</sup>

The outcome of women with a patent ductus arteriosus during pregnancy is mainly dependent of the presence of pulmonary hypertension, this topic is discussed elsewhere in this article. Furthermore, apart from several case reports, no specific data have been reported on this subject.

### Atrioventricular septal defect (AVSD)

Outcome of pregnancy in women with an atrioventricular septal defect (AVSD) is dependent on the presence of left atrioventricular valve regurgitation and presence of ventricular dysfunction. To reduce complications it is advisable to consider valve repair prior to pregnancy in case of severe regurgitation. Some patients with AVSD have complex left ventricular outflow tract obstruction secondary to septal attachments of the left atrioventricular valve. Such obstruction needs careful assessment, and if necessary, relief, before embarking on a pregnancy.

In a report of 62 pregnancies, there was a high occurrence of NYHA deterioration during pregnancy (60.4%), of which 22.9% was persistent for more than a year after delivery, mainly in patients with presence of a residual ASD (with left-to-right shunt). Arrhythmias were reported in 19% of patients, in particular those with a history of arrhythmias. A relatively high neonatal mortality rate of 4.2% was found, directly associated with CHD recurrence in the offspring.<sup>(5,17)</sup>

### Ebstein

Without presence of cyanosis, women with an Ebstein's anomaly undergo pregnancy relatively smoothly. In an article of 1994, describing 111 pregnancies, there were no serious maternal complications reported, arrhythmias did not occur more often than in non-pregnant women. However, neonatal outcome showed several adverse results, including prematurity (27%), lower birth weight (especially in cyanotic women) and fetal mortality (18%).<sup>(5,18)</sup> A recent small retrospective study, showed that NYHA classification and severity of tricuspid regurgitation before onset of pregnancy are of predictive value for outcome after gestation.<sup>(19)</sup>

### Tetralogy of Fallot

Cardiac complications such as arrhythmias and symptomatic right heart failure are reported in 12% of these pregnancies. A cohort describing this prevalence, showed no specific predictors for adverse events during pregnancy in patients with repaired Tetralogy of Fallot. However, there tended to be an association between severity of pulmonary regurgitation and symptomatic heart failure.<sup>(20)</sup>

Evidence on outcome of pregnancy in severe pulmonary regurgitation is conflicting, possibly due to small numbers of patients actual embarking pregnancy. Current guidelines suggest considering pulmonary valve intervention before onset of gestation, specifically in patients with dysfunction of the right ventricle.<sup>(5)</sup>

Additionally, in the study of Balci, et al. medication use before pregnancy, showed a negative association with the child's outcome. Arrhythmias were the main cause of maternal events. They occurred most often in patients who had a history of arrhythmias and patients with a prior pulmonary valve replacement. An association between maternal events and fetal outcome was found, i.e. small-for-gestational-age.<sup>(21)</sup>

### Transposition of the great arteries (TGA)

Women treated with a Senning or Mustard procedure have an increased risk of developing cardiac morbidity during pregnancy, such as supraventricular arrhythmias and heart failure. These arrhythmias may be associated with the extensive atrial scarring, being substrate for electrophysiologic disbalance. Spontaneous miscarriages are reported, but data are subject to survival and publication bias. Moreover there are obstetric problems: prematurity, in about 30% of cases, as well as hypertensive disorders associated with pregnancy.<sup>(22)</sup>

Patients present more often with preeclampsia which may be associated with a lower perfusion of the placenta. In these patients this is possibly caused by a decreased ability of the systemic ventricle to meet the demand of pregnancy for an increase of cardiac output. High fetal mortality has been reported: 11.7% compared to 1% in the normal population.<sup>(23)</sup> As there is a lack of specific risk factors to predict this adverse outcome, frequent follow-up of these patients is recommended during gestation. Impaired function of the right ventricle, as well as severe valvular dysfunction, is a valid reason to dissuade pregnancy.<sup>(5)</sup> There are little data on women treated with the more recent approach: the arterial switch operation,<sup>(24)</sup> but outcomes are expected to be better than for the Senning/Mustard approach, since the left ventricle is the systemic ventricle and there is no extensive atrial scarring to act as a substrate for arrhythmia.

## Fontan palliation

Small numbers of pregnant women with a Fontan circulation have been described in literature. In the small series published so far these patients showed a high risk of developing complications (multiple supraventricular tachycardias, NYHA deterioration) as well as hemorrhagic complications and obstetric problems, for instance prematurity, premature rupture of membranes and neonatal death.<sup>(14)</sup> Fontan patients have a less than favorable outcome when it comes to completion of pregnancy. Miscarriages and abortion rates are higher compared to most of the other congenital heart diseases with about 50% of pregnancies completed.<sup>(22,25)</sup> Guidelines advise against pregnancy in "Fontan patients with depressed ventricular function, moderate to severe atrioventricular valvular regurgitation, with cyanosis or with protein-losing enteropathy".<sup>(5)</sup> As these patients are in WHO IV, this is a group with highest risk of complications. The outcome in more recently operated Fontan patients needs to be awaited and may be more positive.

## Aortic pathology

Due to an increase in cardiac output and hormonal changes affecting the arterial wall, patients with aortic disease have a higher risk of dissection during pregnancy. If a patient's history reveals an earlier dissection or dilatation of the aorta, the (pre-) pregnancy counselling and guidance should definitely be carried out in a specialised center, with cardiovascular surgery available and should include optimal imaging of the entire aorta.

A large review of Immer, et al., aiming to determine predictive factors of aortic dissection, suggests that in all cases, a dilated aorta (larger than 40mm) preferably has to be surgically treated before onset of pregnancy, to minimize the risk of occurrence of dissection.<sup>(26)</sup>

Recent European guidelines are more conservative: they suggest consideration of surgery pre-pregnancy in patients (except for Marfan, as will be discussed) with an aortic dilatation of larger than 50mm. Also, when a patient presents with a dilated aorta during pregnancy, surgery must be considered if the diameter appears to be larger than 50mm or is rapidly progressive.<sup>(5)</sup> In case of an acute dissection type A, advised policy depends on duration of gestation. Under 30 weeks, acute surgery should be done. In case of a pregnancy duration over 30 weeks, an emergency aortic replacement should be preceded by caesarean section.

## Bicuspid aortic valve

Fifty per cent of these patients have a dilated ascending aorta, which should be evaluated preferably before pregnancy to assess

the diameter. Surgery may be required if the aortic diameter exceeds 50mm.

A bicuspid valve is a common underlying mechanism for both aortic stenosis and regurgitation. In asymptomatic severe aortic valve stenosis (valve area  $\leq 1.0\text{cm}^2$ ) with normal ventricular systolic function and a normal exercise test (ie normal capacity, normal blood pressure rise and no ECG changes), appropriate permissive advice can be given: pregnancy is likely to be tolerated with careful specialist monitoring. If the patient is symptomatic or has an abnormal exercise capacity, guidelines suggest pregnancy should be discouraged until the stenosis is treated.<sup>(5)</sup>

The same approach is advised in the case of severe aortic regurgitation, although pregnancy generally is better tolerated as systemic vascular resistance lowers, with a favourable effect on regurgitation. Guidelines on valvular disease suggest consideration of pre-pregnancy surgery, if a patient is symptomatic or has a diminished systolic ventricular function.<sup>(27)</sup>

## Coarctation of the aorta

In coarctation, counselling prior to pregnancy is also important as the patient may need (first or re-) intervention pre-conceptionally. However, whether or not these patients have had an intervention, the risk of aortic rupture or cerebral aneurysm is not zero, especially in those with hypertension. Pregnancy related hypertensive disorders are more frequent in this population. Adequate follow-up of blood pressure is essential. Lowering the blood pressure has to be considered, but with extra caution in pregnant patient, because antihypertensive medication can lower the placental perfusion.<sup>(5,22)</sup>

## Marfan Syndrome

Certain risk factors for dissection during pregnancy in patients with Marfan have been revealed in a large review. An aortic root diameter of more than 40mm and a significant increase in this diameter appeared to be risk factors of dissection.<sup>(26)</sup> If there is a family history of dissection in a patient with Marfan, the risk on dissection is higher. Even in patients who had already undergone an aortic root replacement, there's still an elevated risk of dissection as the whole aorta is involved in the disease process. When the aortic root diameter exceeds 45mm it is advised to perform surgical treatment pre-pregnancy.<sup>(5)</sup>

Recent prospective research conducted in a population of only women with Marfan (aortic root diameter before pregnancy 25-45mm, mean  $37 \pm 5\text{mm}$ ) showed no increased dilatation, dissection or rupture of the aorta. However, there seems to be a slightly accelerated growth of diameter in pregnant women with an aortic root of  $\geq 40\text{mm}$ . The discrepancy of results might be caused by the large range in diameter included in this cohort.<sup>(28)</sup>

### Pulmonary valve stenosis or regurgitation

Severe pulmonary valve dysfunction (stenosis or regurgitation) can lead to maternal complications such as arrhythmias and heart failure. In addition to the maternal complications there is a variety of general and neonatal complications reported. In pulmonary stenosis, hypertension related disorders were reported in 15% of women, prematurity in 17% and offspring mortality is seen in 4.8% in a cohort of 81 pregnancies. In this study there were three patients, with a corrected stenosis, presenting with a thromboembolic event in the absence of risk factors besides the pregnancy. This finding was not seen in other studies and needs further investigation, before drawing firm conclusions.<sup>(5,29)</sup> Percutaneous pulmonary valvuloplasty can be safely performed in pregnant women with severe pulmonary stenosis and suitable valve morphology.

In case of pulmonary valve regurgitation (with or without associated other defects and whether or not it is combined with an RV outflow obstruction) there has to be awareness of the predictive value of a severe regurgitation with respect to the risk of symptomatic right heart failure.<sup>(30)</sup>

### Pulmonary hypertension, Eisenmenger and cyanosis

A different approach to the patient is needed in all of the above described congenital heart diseases, if pulmonary hypertension (PH), Eisenmenger or cyanosis is present. Risks for adverse outcomes in mother and child are significantly higher and will be explained in this section.

#### Pulmonary hypertension

There is a distinct difference in maternal mortality if the disease is associated with PH, with a mortality rate varying from 17-33%.<sup>(5)</sup> Most patients die peri- or postnatal, with several possible etiologies. It may be due to blood loss and subsequently a volume shift affecting a hypovolemic right ventricle that is prone to failure. It can either be due to pulmonary thrombosis, as pregnancy causes a hypercoagulable status and delivery provokes stasis due to fetal pressure on the vena cava inferior, while PH frequently goes together with pulmonary vascular changes. A combination of these factors contributes to an environment more prone to pulmonary thrombosis. Lastly, the pulmonary vascular resistance increasing during pregnancy in PH patients, and elevating even more during delivery, can also lead to maternal death. Neonatal mortality in this group can be as high as 10-13%.

A clear cutoff value does not exist; even modestly elevated pulmonary artery pressures confer a high risk of maternal death. If a woman with pulmonary hypertension nevertheless wants to proceed with pregnancy, frequent follow-up is advised in a specialised pulmonary hypertension centre, at least monthly. Also, mode and timing of delivery should be discussed and prepared in a multidisciplinary nature beforehand.

Recently a small study reported the pregnancy of 10 patients with pulmonary hypertension. These patients were administered on selected targeted drugs and continued taking these drugs during pregnancy. They tolerated pregnancy relatively well. Teratogenic effects (of some targeted drugs like Bosentan) have to be evaluated and discussed before continuation during pregnancy.

With these recent relatively positive results, further research should be awaited.<sup>(5,31)</sup>

#### Eisenmenger

In Eisenmenger patients the risk for maternal mortality is as high as 20-50% and also fetal outcome is hampered, especially if oxygen saturation is below 85%, with the chance on a live birth being only 12%. A patient should be advised against pregnancy and discontinuation of an ongoing gestation should be offered. However, termination of pregnancy is not without risks either, as anaesthesia is required.<sup>(5,22)</sup>

#### Cyanosis

In women with a persistent right-to-left shunt, surviving to reproductive age without significant pulmonary hypertension, risks during pregnancy are dependent on the oxygen saturation. In a cohort of 44 women (96 pregnancies) it was demonstrated that if the oxygen saturation was 90 % or more, then there was a 92% chance that the pregnancy would be successful. Also they can tolerate pregnancy relatively well, although in the overall group there were a lot of heart failure presentations. But neonatal outcome is definitely impaired if oxygen saturation is lower than 85%: in 17 pregnancies only 2 neonates survived.<sup>(32)</sup> So baseline oxygenation before pregnancy is an important factor to take into account in women with cyanotic congenital heart disease. Guidelines advise performing an exercise test to objectively assess possible decrease in saturation during exercise.<sup>(5)</sup>

### MEDICATION

The use of medication should always be discussed with future parents. Some medication is potentially toxic to the fetus. Therefore,

Careful consideration has to be made as medication cannot always be simply withdrawn. The woman may have to accept a balance of risk between the risk to the mother (and therefore the fetus) of stopping a drug, versus the risk to the fetus of continuing it. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers should be stopped before the onset of pregnancy because fetal adverse effects have been described, for example oligohydramnion, growth restriction, renal failure due to renal or tubular dysplasia, hypocalvaria (cranial hypoplasia), cardiac defects and even intrauterine fetal death.

Beta-blockers possibly have an effect on the birth weight of the child, although there is uncertainty as to whether this effect could be related to the underlying condition rather than the drug itself. A recent analysis of a large registry found differences in birth weight between the several indications for the use of beta blockade. For instance, a clear effect was found in patients with valvular heart disease or arrhythmias, while no effect was found in patients treated with beta-blockade because of hypertension.<sup>(33)</sup> Also the type of beta blocker may be important; atenolol in particular is considered likely to reduce intrauterine growth.<sup>(5)</sup>

Amiodarone has an effect on the thyroid gland of the fetus. Women on this drug should be withdrawn if possible before pregnancy, however refractory ventricular arrhythmias can be an exception for this.<sup>(34)</sup> The long half life of amiodarone means that stopping it during a pregnancy may not benefit the fetus – it is still exposed to the drug.

Advice for the use of Vitamin K antagonists differ depending on the trimester. The fetus is at risk of teratogenicity during the 1st trimester, and of intracerebral bleeding throughout the pregnancy and delivery. Clear, concise advice is hard to give, but the European Society of Cardiology<sup>(5)</sup> has gone to great efforts to provide guidelines, especially concerning patients with mechanical valves. When a patient is taking a Vitamin K antagonist in week 6-9, the risk of developing embryopathy is about 6% and is probably related to the dose. The decision on anticoagulation should be made together with the patient after explaining the options to the patient and her partner. The options include continuing the oral anticoagulation if the patient uses a relatively low dosage (<5mg warfarin, <3mg phenprocoumon, <2mg acenocoumarol) or switching to (low molecular weight) heparin from the 6th week until the 12th week of gestation if there is a need for a relatively high dosage (>5mg, >3mg, > 2mg respectively). If there has been a choice to discon-

tinue the vitamin K antagonist, anticoagulation can be switched to either low molecular weight heparin (with an anti-Xa check weekly) or unfractionated heparin (at least twice daily check of aPTT). The decision also depends on the indication for anticoagulation (for instance type and position of a mechanical valve). In the second trimester a patient can be restarted on oral anticoagulation. In the third trimester it's advisable to again switch to LMWH or UFH at 36 weeks. Thirty-six hours before delivery LMWH should then be switched to UFH, as it can be stopped several (4-6) hours before the delivery, and restarted 4-6 hours after (if there is no significant hemorrhage).<sup>(5)</sup>

### MODE OF DELIVERY

Mode of delivery should be discussed early in pregnancy preferably with a specialised team consisting of cardiologists, obstetricians and anesthesiologists with expertise in this field. Vaginal delivery is considered the mode of choice in most patients with congenital heart disease. Exceptions should be made for women with aortic disease involving an aortic root diameter of more than 45 mm or dissection in the past, women who were administered on oral anticoagulation during onset of labour or women in acute heart failure or acute aorta dissection.<sup>(5)</sup>

Caesarean section (CS) is associated with more obstetric complications such as thromboembolic events, infection and hemorrhage.<sup>(35)</sup> In a recent prospective cohort of 1 262 women with structural cardiac disease (67% congenital heart disease) vaginal delivery appears at least as good as CS (with no clear difference in outcome between planned and emergency CS). Moreover, caesarean section is also associated with a higher occurrence of prematurity and a lower birth weight.<sup>(36)</sup>

Guidelines prefer vaginal delivery for most patients, with epidural anaesthesia for continuous pain management, to limit the haemodynamic changes in the actual delivery.<sup>(5)</sup>

Infective endocarditis is rarely seen during pregnancy in congenital heart disease. With a lack of evidence on association between endocarditis and pregnancy or delivery, the guidelines advise no additional endocarditis prophylaxes during vaginal delivery or caesarean section. Selected patients with a prosthetic valve or prosthetic material for valve repair, patients who have had previous endocarditis and patients with cyanotic congenital heart disease without surgical repair, with residual defects or palliative shunts or conduits are at high risk. If congenital heart disease is repaired with prosthetic material, it is advisable to prescribe prophylaxis for up to 6 months after the intervention.<sup>(37)</sup>

## RECURRENCE RISK

Rate of recurrence is a disease-specific topic. In Table 3, recurrence rates are listed.<sup>(17,18,20,38-43)</sup>

## FEATURE RESEARCH

The majority of current evidence on pregnancy in adult congenital heart disease consists of relatively small cohorts and case series. Subsequently, publication and selection bias have to be taken into account. Large prospectively studies are needed for future research to increase our knowledge on this important topic. The Registry on Pregnancy and Structural Heart Disease (ROPAC) was initiated to observe a large number of women during pregnancy, with preliminary structural heart disease, including congenital disorders, but also patients with valvular heart disease, cardiomyopathy, ischaemic heart disease, aortic disease or pulmonary hypertension can be included. By collecting data in this registry, we can provide a solid foundation for further risk stratification and may form the basis for randomised controlled trials.<sup>(44)</sup> Information about this registry can be found at: <http://www.escardio.org/guidelines-surveys/eorp/surveys/pregnancy>.

## CONCLUSION

In most women with congenital heart disease, pregnancy is well tolerated, although there should be awareness of cardiac, obstetric

and neonatal risk. If a patient presents with the wish to become pregnant, she should be referred to a specialised center and the parents should get extensive information on these risks. Using WHO classification, one can identify women at high risk. The most frequent cardiac complications are heart failure and arrhythmias. When cardiac events occur, there is a higher risk of complications for the offspring as well. Continuing to carry out research in this field is important for providing these women the best evidence based clinical practice.

**Conflict of interest: none declared.**

**TABLE 3:** Recurrence risk of congenital heart disease in offspring: Affected mother.<sup>(17,18,20,22,38-43)</sup>

Congenital heart disease	Recurrence risk
ASD	4.5-6%
VSD	6-9.5%
PDA	4%
AVSD	7.5-15%
Ebstein	3.9 - 6%
Tetralogy of Fallot	2.5-10%*
TGA	0.5%**
Bicuspid aortic valve	4.1-9.3%***
Aortic coarctation	4%
Marfan	50%
Pulmonary valve stenosis	7%

ASD = Atrial Septal Defect. VSD = Ventricular Septal Defect. PDA = Patent Ductus Arteriosus. AVSD = Atrioventricular Septal Defect. TGA = Transposition of Great Arteries.

\* Range varies to 50% if associated with for instance 22q11.2 deletion.

\*\* Total recurrence risk, affected mother or father.

\*\*\*Approximate risk, based on:

- recurrence risk of CHD in aortic stenosis is approximately 4.1-5% (regardless of bicuspid or tricuspid);

- Bicuspid valves: 4.6%, 9.1 and 9.3% recurs in first degree family overall.



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