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SPECIAL ARTICLE

Pre-pregnancy risk assessment and counselling of the cardiac patient

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Abstract Pregnant women with heart disease often have an increased risk of maternal cardiovascular and offspring complications. The magnitude of these risks varies depending on the type and severity of the underlying disease. Therefore risk assessment should be performed before pregnancy. This can be accomplished by taking into account predictors and risk scores that have been developed in large populations of pregnant women with heart disease, as well as by consulting disease-specific pregnancy literature. A system that integrates all available knowledge about the risk of pregnancy is the adapted World Health Organisation risk classification. The safety of pregnancy for women with heart disease can be enhanced by adequate risk assessment and counselling.

Keywords Pregnancy · Heart disease · Risk · Counselling

Introduction

The prevalence of maternal heart disease during pregnancy is estimated at 0.5–1% and is increasing. While rheumatic heart disease is most prevalent in developing countries, in the Western world congenital heart disease (CHD) constitutes 80% of maternal heart disease [1, 2]. Pregnancy induces haemodynamic changes (increased intravascular volume and cardiac output, decreased systemic vascular resistance and hypercoagulable state) which are associated with increased risk for mother and foetus when maternal heart disease is present. In the UK, heart disease is now the most important cause of maternal death, and in the Netherlands it is the most frequent indirect cause [3]. Many deaths occurred in women who were previously not known to have heart disease, and substandard care contributed in many cases. A high level of suspicion for heart disease may therefore prevent fatal outcome. Maternal mortality is, however, just the tip of the iceberg: maternal morbidity and offspring morbidity and mortality are far more important numerically. The most prevalent maternal cardiovascular complications that occur during pregnancy are heart failure, arrhythmias, thromboembolic events, and aortic dissection. In women with a known history of heart disease, full investigation pre-pregnancy and expert risk assessment and counselling are extremely important. This prevents women from embarking on pregnancy when the risk for their lives is high, it allows for interventions to be carried out before pregnancy if necessary, and a management plan can be timely established for the many women who can be expected to go through a relatively safe pregnancy. Our knowledge concerning pregnancy complications and risk estimation in women with heart disease has increased over the years, thus contributing to improved counselling of these women and better care during their pregnancies. This article reviews the recent literature on this subject.

Pregnancy complications and prediction of maternal outcome

Predictors and risk scores

Independent predictors of maternal cardiovascular complications during pregnancy have been identified in recent and older studies [1, 4–8]. An overview of these predictors is presented in Table 1. In addition to previously recognised

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Table 1 Predictors of maternal cardiovascular complications during pregnancy

Predictor	Study	Population	Risk points
CARPREG			
Prior cardiac event (heart failure, transient ischaemic attack, stroke, arrhythmia)	CARPREG	CHD, AHD	1
NYHA functional class III/IV or cyanosis (SO^2 <90%)	CARPREG	CHD, AHD	1
Left heart obstruction (mitral valve area <2 cm² or aortic valve area <1.5 cm² or peak LVOT gradient >30 mmHg (echocardiography)	CARPREG	CHD, AHD	1
Reduced systemic ventricular systolic function (EF <40%)	CARPREG	CHD, AHD	1
ZAHARA			
Prior arrhythmia	ZAHARA	CHD	1.50
NYHA functional class III/IV	ZAHARA	CHD	0.75
Left heart obstruction (peak LVOT gradient >50 mmHg or aortic valve area <1.0 cm²	ZAHARA	CHD	2.50
Mechanical valve prosthesis	ZAHARA	CHD	4.25
Systemic AV valve regurgitation (moderate/severe)	ZAHARA	CHD	0.75
Pulmonary AV valve regurgitation (moderate/severe)	ZAHARA	CHD	0.75
Cardiac medication before pregnancy	ZAHARA	CHD	1.50
Cyanotic heart disease (corrected and uncorrected)	ZAHARA	CHD	1.00
OTHER STUDIES			
Prior cardiac event (heart failure, transient ischaemic attack, stroke, arrhythmia)	Tanous	CHD, AHD	
NYHA functional class III/IV	Song	CHD	
	Kovavisarach	CHD, AHD	
Cardiac medication before pregnancy	Tanous	CHD, AHD	
Anticoagulation therapy	Tanous	CHD, AHD	
Pulmonary arterial hypertension	Song	CHD	
Maximum BNP >100 pg/ml	Tanous	CHD, AHD	
Smoking history	Khairy	CHD	
Reduced subpulmonary ventricular function and/or severe pulmonary regurgitation	Khairy	CHD	
Right ventricular dilataton	Song	CHD	

CARPREG risk score: For each CARPREG predictor that is present, 1 point is assigned to the pregnancy. The risk score is the total number of points. The risk of maternal cardiovascular complications is 5% with 0 points, 27% with 1 point and 75% with ≥1 point

ZAHARA risk score: For each ZAHARA predictor that is present, a predictor-specific number of points is assigned to the pregnancy, according to the table. The risk of maternal cardiovascular complications is 2.9% with <0.5 points, 7.5% with 0.5–1.5 points, 17.5% with 1.51–2.50 points, 43.1% with 2.51–3.5 points and 70% with >3.5 points. AHD=acquired heart disease; AV=atrioventricular; BNP=B-type natriuretic peptide; CHD =congenital heart disease, EF=ejection fraction, LVOT=left ventricular outflow tract, NYHA=New York Heart Association

predictors of adverse outcome such as functional class, left ventricular outflow tract obstruction, cyanosis, arrhythmias, ventricular dysfunction, pulmonary hypertension and mechanical valve prosthesis, several new predictors have come forward in recent studies. The use of cardiac medication pre-pregnancy predicted cardiovascular complications in two studies [7, 8] and is most likely a surrogate marker for severity of heart disease. Also, in CHD, underlying corrected or uncorrected cyanotic heart disease was associated with maternal outcome which probably reflects greater complexity of the underlying lesion. This is in line with a large systematic review concerning pregnancy and CHD [9]. Atrioventricular valvular regurgitation (mitral or tricuspid regurgitation) emerged as an independent predictor of maternal cardiac complications in a large retrospective study, despite the beneficial effect of decreasing vascular resistance during pregnancy. The large population may have allowed weaker predictors of complications to be identified. Additionally, some of the patients had complex underlying heart disease and compromised ventricular function which possibly added to the complication rate [7].

A potentially useful new predictor of maternal cardiac events is B-type natriuretic peptide (BNP). Importantly, BNP (≤100 pg/ml) (mainly obtained during the first trimester) had a negative predictive value of 100% for adverse cardiac events [8]. More data concerning NT-proBNP in pregnant women with heart disease can be expected in the near future [10]. In 2001, the CARPREG investigators presented a risk score to estimate maternal cardiovascular risk of complications in women with acquired

or congenital heart disease [1] (Table 1). In recent years, several studies have validated this risk score [2, 7, 11]. The CARPREG risk score does identify pregnancies with higher risk, but overestimates the actual risk according to most studies (Table 2). The ZAHARA investigators recently published a risk score developed in a large population with CHD [7] (Table 1). This risk score was prospectively validated in the ZAHARA II study and performed better in a population with CHD than the CARPREG risk score [12].

It is important to realise the limitations of predictors and risk scores. They are highly population-dependant: the magnitude as well as the composition of the population determine which predictors will emerge in a certain study. Given the heterogeneity of the population of pregnant women with heart disease, especially in Western countries with a high percentage of CHD, these limitations are of practical importance. To illustrate this, the CARPREG and ZAHARA risk scores failed to identify pulmonary arterial hypertension and dilated aorta as predictors of pregnancy outcome: low prevalence of these predictors is the likely explanation.

Therefore, to estimate the risk of pregnancy, these predictors and risk scores are just one of the tools that must be used. Additionally, disease-specific information should always be taken into account.

Disease-specific information

Congenital heart disease

Most women with congenital heart disease tolerate pregnancy well. The risk of cardiovascular complications increases with increasing complexity of the underlying disease. This is illustrated in a large review that included 2491 pregnancies [9]. This review provides the incidence of cardiovascular complications (heart failure, arrhythmias and cardiovascular events separately) for 14 congenital heart disease diagnoses and can be used as a quick reference. While cardiac complications are rare (<5%) in women with atrial or ventricular septal defect and pulmonary stenosis, they occur frequently (>15%) in women with transposition of the great arteries, Eisenmenger syndrome, Fontan circulation and uncorrected or palliated cyanotic heart disease. In women with an atrioventricular septal defect, atrial correction of transposition, tetralogy of Fallot and Fontan circulation, arrhythmias are the most frequent complication. In aortic stenosis, pulmonary atresia with ventricular septal defect and uncorrected or palliated cyanotic heart disease, heart failure is the main complication [9].

Valvular heart disease

Mitral stenosis is the most frequent cardiac diagnosis in pregnant women with rheumatic heart disease and is not well tolerated during pregnancy [1, 5, 13]. Even moderate mitral stenosis predicts worse outcome and should be treated interventionally before pregnancy [1, 13]. Aortic stenosis in pregnant women is mostly congenital in origin and, according to recent studies, is better tolerated than previously thought, even when it is severe [14]. Symptomatic aortic stenosis should, however, be corrected before pregnancy. The choice of valve prosthesis should then be carefully considered. Bioprostheses have a low complication rate during pregnancy but valve degeneration, ultimately leading to reoperation, is a problem in women at young age. The Ross operation may be an alternative in experienced hands. Data on pregnancy after the Ross operation are scarce, but promising [15]. Mechanical prostheses carry a high complication rate. The most important complication is valve thrombosis. In the Dutch ZAHARA I study, even though the prevalence of pregnancies with a mechanical valve was low, the presence of a mechanical valve was still the strongest predictor of maternal complications [7] (Table 1). The necessity for anticoagulation therapy raises the dilemma to continue vitamin K antagonists throughout the first trimester with a relatively low risk of valve thrombosis (±2%) but with the risk of embryopathy (on average 6%), or to eliminate the risk of embryopathy by substituting the oral anticoagulant with unfractionated or low-molecular-weight heparin and accept a higher risk of valve thrombosis. Expert opinion diverges on this subject. An open and full discussion with the mother-to-be should already take place before pregnancy. Such a discussion should make clear that the foetus is not only threatened by embryopathy, but also by valve

Table 2 External validation of the CARPREG risk score for cardiovascular complications in pregnancy in women with heart disease

CARPREG *N*=599	Khairy *N*=90	Curtis *N*=177	ZAHARA *N*=1302	Tanous *N*=66	Jastrow *N*=312
Risk score–% complications	% complications				
0–5%	12	5	6	2	1.4
1–27%	30	18	16	30	19
≥1–75%	100	57	22	50	–

LVOT left ventricular outflow tract, *NYHA* New York Heart Association

thrombosis, which may cost the lives of both mother and foetus or which may lead to foetal neurological damage when acute valve surgery is necessary during pregnancy. The risk of foetal complications is low when the use of oral anticoagulant therapy is avoided in the first trimester. Therefore the new European Society of Cardiology (ESC) guidelines [13] recommend vitamin K antagonists as the anticoagulation of choice in the 2nd and 3rd trimester. Moreover, since the occurrence of embryopathy appears to be dose-dependant, it is recommended to consider continuation of oral anticoagulants when the dose requirement is low (i.e. warfarin <5 mg daily which is equivalent to acenocoumarol <2 mg daily). With higher dose requirements, unfractionated heparin or low-molecular-weight heparin can be used from week 6–12. Strict control of the anticoagulation effect is necessary. For unfractionated heparin, APTT >2 times control is advised. When low-molecular-weight heparin is used, anti-factor Xa levels need to be monitored. However, optimal peak anti-factor Xa levels are not known; usually the recommendation is 0.8–1.2 U/l 4 h post-dose. Since rise of glomerular filtration rate during pregnancy can cause pre-dose levels to be low even when peak anti-factor Xa levels are adequate, there is an argument for additional monitoring of pre-dose levels, but data on the consequences of pre-dose level monitoring in pregnant women with mechanical valves are lacking.

Aortic disease

Women with aortic dilatation based on underlying Marfan syndrome have a high risk of dissection during pregnancy when the aortic diameter is >45 mm. Pre-pregnancy surgery is then recommended. When aortic diameter is <40 mm pregnancy is relatively safe. In women with bicuspid aortic valve and aortic dilatation, a pre-pregnancy diameter of >50 mm is considered a contraindication for pregnancy [13].

Cardiomyopathy

Disease-specific information on cardiomyopathies is summarised in a recent review and in the ESC guidelines [13, 16]. Hypertrophic cardiomyopathy is often well-tolerated. The occurrence of complications is mainly dependant on pre-pregnancy NYHA class and on left ventricular outflow obstruction. In dilated cardiomyopathy the risk of pregnancy is dependant on pre-pregnancy NYHA class and on left ventricular function.

Risk for the offspring

Not only maternal cardiac events, but also offspring events occur more often in women with heart disease. Premature delivery, too low birth weight for the gestational age, offspring mortality and congenital heart disease occur more often compared with healthy women. Maternal and offspring events appeared to be highly related in the ZAHARA I study (r=0.85) [7]. Comparable to maternal cardiovascular events, offspring events appear to be dependant on disease complexity [9]. Predictors for offspring events that have been identified in the CARPREG and ZAHARA I studies are multiple pregnancy, smoking during pregnancy, NYHA class III/IV, left heart obstruction, heparin/warfarin during pregnancy, other cardiac medication during pregnancy, cyanosis and a mechanical valve prosthesis [1, 7].

Risk estimation: an integrated approach

A system that integrates all available knowledge was proposed by an English group of experts. They adapted the World Health Organisation (WHO) classification for use of contraceptive methods to classify the maternal risk of pregnancy associated with specific cardiovascular conditions [17]. Pregnancies are classified into four categories (WHO class I-IV): low, medium and high risk of pregnancy as well as contraindication for pregnancy. This classification combines the knowledge of disease-specific literature with the predictors of pregnancy outcome known at that time. The authors provide a collection of tables that apply the classification in a practical way. Examples of conditions with low risk (WHO I) are mild pulmonary stenosis or surgically corrected ventricular or atrial septal defect. A contraindication to become pregnant (WHO IV) is present in women with pulmonary arterial hypertension, severe systemic ventricular dysfunction, severe mitral stenosis, severe symptomatic aortic stenosis, Marfan syndrome with aortic dilatation >45 mm, and peripartum cardiomyopathy with residual ventricular dysfunction. Women with a mechanical prosthetic valve, a systemic right ventricle, unrepaired cyanotic disease or Fontan circulation have a high risk (WHO III). For most other diagnoses, it depends on the severity of the valvular or ventricular dysfunction and the presence of one or more diagnoses whether they are assigned to WHO class II or to class III. Therefore, in some cases expert experience and knowledge will influence the classification.

The adapted WHO classification was the most accurate system for risk evaluation in a prospective evaluation of several risk estimation models [12]. It is advocated in the new ESC guidelines for the management of cardiovascular diseases during pregnancy as the risk estimation system of choice [13]. Management advice is assigned to these risk classes. While for women with low or moderate risk (WHO class I or II) cardiology follow-up can be limited to once per trimester or even less, women in WHO

class III and IV have a high or very high risk. These women benefit from frequent control (monthly or bimonthly) in a specialised centre.

Counselling of women with heart disease

The counselling of cardiac patients about the risk of pregnancy should commence as soon as they become sexually active. Especially girls who have a high risk should be notified about the necessity to plan future pregnancies carefully. Adequate advice concerning contraception should be offered. At this young age it will not be necessary to give detailed information about pregnancy, but the paediatric cardiologist must repeatedly discuss the need to use a reliable contraceptive. After transition to adult cardiology the young woman should again be reminded to discuss her pregnancy wish with her cardiologist before actually getting pregnant. When a woman wants to get pregnant, clinical assessment including echocardiography, exercise testing and sometimes 24-hour ECG and MRI is indicated. Based on these data, risk assessment can be performed. When it is decided that the woman can carry on and attempt to get pregnant, each medicine that she is using should be reviewed: is it necessary to continue this medication throughout pregnancy, or can it be safely discontinued, or should it be replaced by a safer alternative? A plan for cardiology and obstetric supervision during pregnancy must be made: when and where should the woman be seen for the first time by these specialists? When the heart disease has a genetic basis referral to a geneticist is often indicated. Finally, normal pregnancy care, such as the advice to start folic acid, should not be forgotten.

In conclusion, many women with heart disease can go through pregnancy with few or no complications. The safety of pregnancy for women with heart disease can be enhanced by adequate risk assessment and counselling.

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