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THE PRESENT AND FUTURE

STATE-OF-THE-ART REVIEW

# High-Risk Cardiac Disease in Pregnancy

## Part I

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**ABSTRACT**

The incidence of pregnancy in women with cardiovascular disease is rising, primarily due to the increased number of women with congenital heart disease reaching childbearing age and the changing demographics associated with advancing maternal age. Although most cardiac conditions are well tolerated during pregnancy and women can deliver safely with favorable outcomes, there are some cardiac conditions that have significant maternal and fetal morbidity and mortality. The purpose of this paper is to review the available published reports and provide recommendations on the management of women with high-risk cardiovascular conditions during pregnancy. (J Am Coll Cardiol 2016;68:396–410)


Cardiovascular disease has been estimated to be present in 1% to 4% of pregnancies. The incidence of pregnancies in women with heart disease is rising, mainly due to an increased number of women with congenital heart disease (CHD) reaching childbearing age; advancing maternal age; and increased incidence of risk factors, including diabetes mellitus, hypertension, pre-eclampsia, and multifetal pregnancies.

Although the majority of women with cardiac disease can become pregnant and, with early diagnosis and appropriate management, can be brought to term safely, there are high-risk cardiac conditions that may be associated with important morbidity, and even mortality. With increased numbers of pregnancies in women with cardiac problems, heart disease has emerged as the leading cause of nonobstetric maternal mortality. This state-of-the-art review is focused on the approach to pregnancy in women with cardiac conditions associated with high maternal and fetal risks (**Central Illustration**).

## NORMAL CARDIAC PHYSIOLOGY OF PREGNANCY

Blood volume increases substantially during pregnancy, starting as early as the sixth week and rising rapidly until midpregnancy, when the rise continues at a slower rate, with an average maximum increase of 50% (1,2) (**Figure 1**). Because the red blood cell mass increases less rapidly, the hemoglobin concentration falls, causing the "physiological anemia of pregnancy." Cardiac output (CO) during pregnancy increases by about 50%, predominantly due to augmentation of stroke volume during early pregnancy and increased heart rate in the third trimester. Systemic blood pressure (BP) falls during the first trimester, reaching a nadir in midpregnancy and returning toward pre-gestational levels before term. This change results from a decline in systemic vascular resistance due to reduced vascular tone. Hemodynamics are altered substantially during labor and delivery, secondary to anxiety, pain, and uterine

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contractions. Oxygen consumption increases 3-fold, and systolic and diastolic BP rise during contractions. Reduction of pain and apprehension with analgesia and anesthesia may limit hemodynamic changes and the rise in oxygen consumption. Cesarean delivery is frequently recommended in women with cardiac disease; however, it can be also associated with considerable hemodynamic changes related to intubation and drugs used for anesthesia. A temporary increase in intracardiac pressures may occur immediately after delivery due to relief of caval compression and blood shift from the contracting uterus into the systemic circulation, which may lead to clinical deterioration.

## PREGNANCY RISK ASSESSMENT

Assessment of pregnancy risk is an important aspect of the care of women with heart disease who are of childbearing age (3). All women with cardiac disease can benefit from pre-conception counseling, which should include a detailed discussion of the risk of pregnancy. Some women may require optimization of cardiac status prior to pregnancy, and for those women considering pregnancy, cardiac medications that are teratogenic, such as warfarin and angiotensin-converting enzyme inhibitors, can be switched to safer medications when necessary. Increasing numbers of women with heart disease are considering fertility therapy, and in this circumstance, pre-conception risk stratification and safety of fertility therapy should be addressed. A discussion of safe contraception choices is relevant for those who decide not to become pregnant. It is important that this information is communicated effectively to patients; a number of groups have shown that many women do not fully understand pregnancy and contraception risks (3–5).

Cardiologists with expertise in pregnancy and heart disease should perform pre-conception counseling and risk stratification. Issues to address at the time of pre-conception counseling are shown in **Table 1**. Risk assessment should include a complete history and physical examination, a 12-lead electrocardiogram (ECG), and a transthoracic echocardiogram. In women who are pregnant, signs and symptoms of pregnancy can mimic heart disease, and should be interpreted accordingly. Risk stratification may be further defined by incorporating other clinical and imaging information, including disease activity, cardiac computed tomography (CT), or cardiac magnetic resonance. Cardiac magnetic resonance and CT findings should be reviewed and incorporated into risk assessment, especially in women with aortopathies and complex congenital lesions. Exercise stress testing to measure functional capacity and BP response to exercise is useful for risk stratification in women with valve lesions, such as aortic stenosis (AS) (6,7). Cardiopulmonary testing, with measurements of oxygen saturation, functional capacity, peak $VO_2$, and chronotropic index, provides helpful information in women with complex CHD (8). Baseline and serial serum B-type natriuretic peptide levels during pregnancy can be incorporated into pregnancy assessment in women with the potential to develop heart failure (HF) during pregnancy due to myocardial disease, valvular heart disease, and CHD. In specific cases, women with arrhythmias may benefit from continuous ECG monitoring, exercise testing, or electrophysiology studies. Women with inherited cardiac conditions should have a formal genetic evaluation to discuss transmission of disease to offspring (6,9). Autosomal-dominant cardiac conditions include Marfan, Noonan, William, Holt-Oram, and 22q11 deletion syndromes, as well as some of the inherited arrhythmias (long-QT syndrome) and cardiomyopathies (hypertrophic cardiomyopathy). Women with inherited cardiac conditions who have an identified genetic mutation may wish to explore the option of pre-implantation genetic screening. Assessment with maternal fetal medicine specialists (high-risk obstetricians) to discuss obstetric risk is an important part of pre-conception assessment.

To estimate pregnancy risk, it is important to consider general and lesion-specific risk predictors. General risk predictors are relevant for all women with heart disease and include factors such as cardiac history, functional capacity, and ventricular function. Lesion-specific risks are known for many, but not all, cardiac conditions and are discussed later, in the corresponding sections.

For women with pre-existing heart disease, the most common cardiac complications during pregnancy are arrhythmias, HF, and thromboembolic events (TEs). Early studies on pregnancy risk predictors identified functional class and cyanosis as important determinants of adverse outcomes during pregnancy (10–12). Subsequently, large pregnancy cohorts were assembled, and pregnancy risk indexes were developed (13–19), which are shown in **Table 2**. The first prospective risk index was developed by the CARPREG (Cardiac Disease in Pregnancy) investigators. The CARPREG study examined outcomes in women with congenital and acquired heart disease and identified 4 predictors of adverse maternal

### ABBREVIATIONS AND ACRONYMS

**AC** = anticoagulation

**BPHV** = bioprosthetic heart valve

**CHD** = congenital heart disease

**HF** = heart failure

**LMWH** = low molecular weight heparin

**MPHV** = mechanical prosthetic heart valve

**PHV** = prosthetic heart valve

**SCAD** = spontaneous coronary artery disease

**TT** = thrombolytic therapy

**UFH** = unfractionated heparin