6. Pregnancy in women with cardiomyopathies and primary arrhythmia syndromes

6.1. Cardiomyopathies

Cardiomyopathies are characterized by disease-specific structural abnormalities and increased risk of ventricular and supraventricular arrhythmias. The risk associated with pregnancy in a woman with cardiomyopathy can be estimated using the mWHO 2.0 classification (*Table 6*). Pre-pregnancy, women with cardiomyopathies should be clinically evaluated to optimize treatment, avoid contraindicated drugs, and assess the risk of heart failure and arrhythmias. Indicated procedures, including implantable cardioverter defibrillator (ICD) implantation, should be performed before pregnancy. [60]

Genetic counselling is recommended before pregnancy to explain the probability of genetic transmission, risks for the mother, foetus, and child, and the possibilities of pre-implantation and pre-natal genetic testing (*Table 7*).[60,281] Women with cardiomyopathies should be managed by the Pregnancy Heart Team, including a cardiologist with expertise in cardiomyopathies and arrhythmias.

6.1.1. Dilated cardiomyopathy and non-dilated left ventricular cardiomyopathy

In women with dilated cardiomyopathy (DCM) and non-dilated left ventricle (LV) cardiomyopathy (NDLVC), severe systolic LV dysfunction, New York Heart Association (NYHA) functional class III/IV, RV failure, sustained ventricular arrhythmias, AF, and/or severe mitral valve regurgitation (MR) are high-risk criteria for major adverse cardiovascular events during pregnancy.[282] In contrast, women with mild LV dysfunction, good functional status, no arrhythmias, and no history of cardiac events are likely to have an uncomplicated pregnancy.[282]

Therapy should be modified before pregnancy. ACE-Is, ARBs, mineralocorticoid receptor antagonists (MRAs), sacubitril/valsartan, and SGLT2 inhibitors are all contraindicated during pregnancy. Pre-pregnancy risk stratification should include temporary withdrawal of contraindicated medication with close monitoring (see *Section 12.6* Heart failure). Beta-blockers should be continued with close monitoring of foetal growth. If anticoagulation is needed for AF or evidence of an intracardiac thrombus, LMWH should be used (see *Section 5* for dosing regimens).

Data about genotype-specific management during pregnancy are scarce but one study evaluated the risk of pregnancy and progression of cardiomyopathy in women with lamin A/C (*LMNA*) P/LP variants.[283] A small subset of women experienced arrhythmias during pregnancy although a history of pregnancy was not associated with long-term adverse disease progression.[283]

More information is included in *Sections 7, 12.4*, and *12.6*.

6.1.2. Arrhythmogenic right ventricular cardiomyopathy

Several observational studies and registries have shown that pregnancies in women with arrhythmogenic right ventricular cardiomyopathy (ARVC) are generally well tolerated with good foetal outcomes and no cardiac mortality when receiving optimal surveillance and therapy.[284,285] Delivery was usually vaginal and appeared safe. Sustained ventricular arrhythmias were reported in 5% of pregnancies and HF in 13%. Neither increased arrhythmia burden or ICD shocks were observed.[284] Beta-blocker therapy should be continued during pregnancy (with the exception of atenolol) or could be started in pregnancy if needed. The two most used anti-arrhythmic drugs in previous studies, beside beta-blockers, were flecainide and sotalol. Both drugs have a long record of safety. However, sotalol should be used with caution in women with reduced ejection fraction (EF) and with careful corrected QT interval (QTc) monitoring.[60] Sotalol also has a beta-blocker effect, necessitating monitoring of foetal growth.[286,287] Amiodarone is contraindicated in pregnancy. In women at high arrhythmic risk, an ICD should be implanted, preferably before pregnancy (see *Section 12.4*).

Two large studies of women with ARVC showed that pre-pregnancy phenotypical severity, rather than pregnancy itself, was the primary risk factor. Pregnancy was uneventful in the overwhelming majority.[288,289] Pregnancy did not seem to accelerate long-term progression of the ARVC phenotype.[288]

6.1.3. Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy[290] is the most common inherited cardiomyopathy and is often caused by variants in sarcomeric genes.[60] Phenocopies such as Anderson–Fabry disease and Danon disease[290] are X-linked and therefore the cardiac phenotype tends to be milder and occurs later in life in females than males, making pregnancy usually uneventful.[291–293]

Despite higher maternal mortality in women with HCM compared with the general population, absolute maternal mortality is low (0.5%) and confined to women at particularly high risk (*Table 6*).[294,295] Data from the ROPAC registry showed that despite overall good outcomes, 23% of pregnant women with HCM developed major cardiac events, including VT (10%) and AF (1.7%), mostly in women already identified as high risk prior to pregnancy.[296] A recent systematic review including 1624 women confirmed low neonatal mortality (0.2%) and stillbirths (1%) in pregnant women with HCM.[297] A study including 242 women with HCM found that pregnancy was not a modifier of the long-term outcomes and pregnancy was well tolerated.[298] Risk factors for major adverse cardiovascular events were advanced NYHA class and higher age at diagnosis.[298] Left atrium diameter as a risk factor has been reported with conflicting results.[298,299]

6.1.3.1. Treatment of hypertrophic cardiomyopathy in pregnancy

Ongoing beta-blocker therapy should be continued during pregnancy. Atenolol should be replaced before pregnancy (*Section 5.2.6*). Atrial fibrillation is poorly tolerated in HCM patients in general due to the risk of haemodynamic decompensation, and medical or electrical cardioversion of AF during pregnancy should be considered. Beta-blockers should be started during pregnancy when new symptoms occur [e.g. due to left ventricular outflow tract obstruction (LVOTO)], for rate control in AF, and to suppress ventricular arrhythmias. Verapamil is the second choice of drug when beta-blockers are not tolerated.

6.1.3.2. Left ventricular outflow tract obstruction

Left ventricular outflow tract (LVOT) gradients may increase slightly during pregnancy and were previously associated with increased cardiac events including arrhythmias and HF.[300] However, subsequent studies have not confirmed this association.[296,298]

In women with obstructive HCM, it is recommended to evaluate gradient in basal condition, with exercise and the Valsalva manoeuvre, before pregnancy and with only the medications allowed during pregnancy, to identify those needing septal reduction therapy before pregnancy.[60] Disopyramide may cause uterine contractions and is not recommended in pregnancy and should be discontinued unless the benefits outweigh foetal risk. Data on the safety of alcohol septal ablation during pregnancy are limited to a few case reports.[60,301,302]