



General Clinical Practice Update

Canadian Cardiovascular Society: Clinical Practice Update on Cardiovascular Management of the Pregnant Patient

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ABSTRACT

The number of women of childbearing age with cardiovascular disease (CVD) is growing because of increased survival of children with congenital heart disease. More women are also becoming pregnant at an older age, which is associated with increased rates of comorbidities including hypertension, diabetes, and acquired CVD. Over the past decade the field of cardio-obstetrics has significantly advanced with the development of multidisciplinary cardio-obstetric programs (COPs) to address the increasing burden of CVD in pregnancy. With the introduction of formal COPs, pregnancy outcomes in women with heart

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RÉSUMÉ

Le nombre de femmes en âge de procréer atteintes d'une maladie cardiovasculaire (MCV) augmente en raison du meilleur taux de survie des enfants atteints d'une cardiopathie congénitale. De plus, davantage de femmes sont enceintes à un âge plus avancé, ce qui est associé à des taux accrus de comorbidités comme l'hypertension, le diabète et la MCV acquise. Au cours de la dernière décennie, le domaine de la cardiologie obstétrique a fait des progrès considérables avec l'apparition de programmes de cardio-obstétrique (PCO) multidisciplinaires visant à répondre au fardeau croissant des MCV chez les

pregnant at an older age and thus carry increased rates of comorbidities including hypertension, diabetes, and acquired CVD.¹ Although many women with CVD will consider pregnancy, it is important that they have preconception counselling to clarify the level of risk imposed by pregnancy for them and their offspring.²⁻⁴ In a large contemporary cohort managed at 2 Canadian multidisciplinary cardio-obstetric programs (COPs), 3.5% of pregnancies were complicated by serious cardiovascular events with the most frequent being cardiac death/arrest, heart failure (HF), arrhythmias, and urgent cardiac interventions.⁵ Maternal cardiac mortality remains a concern and there is still much work to do because it is often preventable.^{5,6}

Over the past decade the field of cardio-obstetrics has significantly advanced with the development of multidisciplinary COPs to address the increasing burden of CVD in pregnancy (Fig. 1).⁷⁻⁹ With the introduction of formal COPs, pregnancy outcomes in women with heart disease have improved.³ COPs provide preconception counselling, antenatal and postpartum cardiac surveillance, labor and delivery planning, and are informed by our enhanced understanding of pregnancy risks, disease pathogenesis, and treatment options. The development of risk prediction tools coupled with a better understanding of the effect of pregnancy on specific cardiac conditions has led to better risk stratification.^{2,3} Fresh

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This statement was developed following a thorough consideration of medical literature and the best available evidence and clinical experience. It represents the consensus of a Canadian panel comprised of multidisciplinary experts on this topic with a mandate to formulate disease-specific recommendations. These recommendations are aimed to provide a reasonable and practical approach to care for specialists and allied health professionals obliged with the duty of bestowing optimal care to patients and families, and can be subject to change as scientific knowledge and technology advance and as practice patterns evolve. The statement is not intended to be a substitute for physicians using their individual judgement in managing clinical care in consultation with the patient, with appropriate regard to all the individual circumstances of the patient, diagnostic and treatment options available and available resources. Adherence to these recommendations will not necessarily produce successful outcomes in every case.

disease have improved. COPs provide preconception counselling, antenatal and postpartum cardiac surveillance, and labor and delivery planning. Prepregnancy counselling in a COP should be offered to women with suspected CVD who are of childbearing age. In women who present while pregnant, counselling should be performed in a COP as early as possible in pregnancy. The purpose of counselling is to reduce the risk of pregnancy to the mother and fetus whenever possible. This is done through accurate maternal and fetal risk stratification, optimizing cardiac lesions, reviewing safety of medications in pregnancy, and making a detailed plan for the pregnancy, labor, and delivery. This Clinical Practice Update highlights the COP approach to prepregnancy counselling, risk stratification, and management of commonly encountered cardiac conditions through pregnancy. We highlight “red flags” that should trigger a more timely assessment in a COP. We also describe the approach to some of the cardiac emergencies that the care provider might encounter in a pregnant woman.

insights have been gained into the pathobiology of conditions such as peripartum cardiomyopathy (PPCM) and pregnancy-associated myocardial infarction. There have been multiple advances in medical (eg, vasodilators for pulmonary hypertension [PHT] and interventional (eg, ablation without use of fluoroscopy, percutaneous valve intervention) care for pregnant women.

Canadian COPs exist in almost every province and act as regional referral centres (Supplemental Table S1). Although Canada has a publicly funded health care system created to provide universal health services, geographic, socioeconomic, racial, and ethnic disparities continue to affect health outcomes. In a geographically large and diverse country such as Canada, novel methods of care delivery, including virtual visits and satellite clinics need to be used.

In addition to this Clinical Practice Update, guidelines and position statements on the care of pregnant women with CVD have been issued from the European Society of Cardiology,¹⁰ the American Heart Association,^{11,12} and the American Society of Obstetrics and Gynecology.¹³ Care providers should consider referring any woman with suspected CVD who is considering pregnancy or is pregnant to a COP. This Clinical Practice Update highlights, as reference for care providers, the COP approach to prepregnancy counselling, risk stratification, and management through pregnancy. Special attention is also drawn to the lesions most commonly encountered by care providers in the community. We highlight “red flags” that should trigger a more timely assessment in a COP. We also describe the approach to some of the cardiac emergencies that the care provider might encounter in a pregnant woman.

Approach to the Pregnant Woman With CVD

Physiologic changes of pregnancy

Pregnancy is associated with progressive increases in red cell and plasma volume and heart rate, resulting in an

femmes enceintes. Avec l'arrivée des PCO officiels, les issues de grossesse des femmes atteintes d'une maladie cardiaque se sont améliorées. Les PCO offrent des consultations préconception, une surveillance cardiaque prénatale et post-partum, ainsi qu'une planification de l'accouchement. Les consultations prégrossesse dans un PCO devraient être offertes aux femmes chez qui l'on soupçonne une MCV et qui sont en âge de procréer. Pour les femmes qui consultent alors qu'elles sont déjà enceintes, les consultations devraient se tenir dans un PCO le plus tôt possible dans la grossesse. L'objectif des consultations est de réduire les risques liés à la grossesse à la fois pour la mère et le fœtus lorsque possible. Cela se fait par une stratification du risque maternel et fœtal précise, l'optimisation des lésions cardiaques, l'examen de l'innocuité des médicaments pris durant la grossesse, et l'élaboration d'un plan détaillé pour la grossesse, le travail et l'accouchement. Cette mise à jour de la pratique clinique souligne l'approche des PCO à l'égard des consultations prégrossesse, de la stratification du risque et de la prise en charge des maladies cardiaques fréquemment observées durant la grossesse. Nous mettons en évidence les signaux d'alarme qui nécessitent une évaluation plus rapide dans un PCO. Nous décrivons aussi l'approche à privilégier à l'égard de certaines urgences cardiaques que les prestataires de soins pourraient voir chez les femmes enceintes.

approximate 40% increase in cardiac output, which peaks in the third trimester. The decrease in vascular resistance and systemic blood pressure is maximal during the second trimester. During labor, cardiac output increases further, and is only partially blunted by regional anesthesia. After delivery, with cessation of caval compression by the uterus, an increase in venous return from lower extremities transiently increases cardiac output. Cardiac output does not fully return to baseline until the sixth postpartum month. Alterations in protein binding, and hepatic and renal function modify pharmacokinetics during the ante- and postpartum period. Increased clotting factor production and reduced fibrinolytic activity result in a prothrombotic state.

Pregnancy complications in women with cardiac disease

Pregnancy-associated changes can lead to decompensation in women with previous CVD. A prospective Canadian study reported cardiovascular complications in 16% of pregnancies; HF and arrhythmias were the most common complications; maternal mortality was < 1%.³ HF is most likely to occur in the second or third trimester or in the postpartum period.¹⁴

In addition to cardiac complications, pregnant women with CVD are at increased risk for obstetric (gestational hypertension and postpartum hemorrhage), and fetal and neonatal complications (preterm birth, intrauterine growth restriction). The probability of transmission of CHD to the fetus can range from 3% to 50% depending on the type of parental CHD.^{15,16} This is higher than the 1% risk in offspring born to parents without CHD.

Counselling before and during pregnancy

Prepregnancy counselling in a COP should be offered to women with suspected CVD including structural, electrical, and coronary heart disease. In women who present while pregnant, counselling should be performed in a COP as early as possible in pregnancy.⁵ The purpose of counselling is to

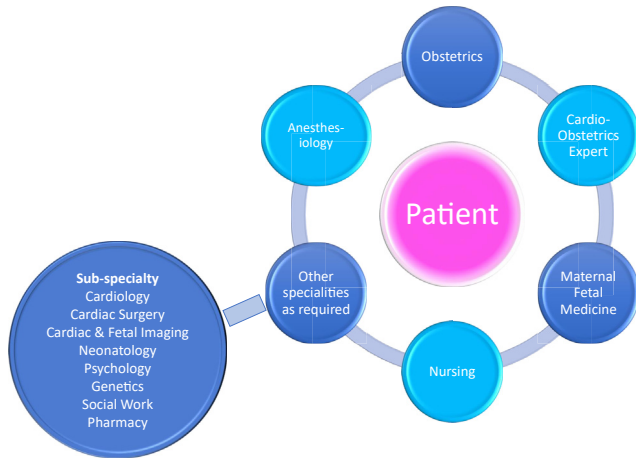


Figure 1. Multidisciplinary cardio-obstetrics team.

reduce the risk of pregnancy to the mother and fetus whenever possible. This is done through accurate maternal and fetal risk stratification, optimizing cardiac lesions, discussing possible pre-pregnancy interventions, reviewing safety of medications in pregnancy, and making a detailed plan for the pregnancy, labor, and delivery.^{3,5,17} Care providers should consider referring any woman with suspected CVD who would benefit from pre-pregnancy counselling or who is pregnant to a COP.

Management planning. Risk stratification in a woman with CVD requires a nuanced approach and is best undertaken in a COP. It is helpful for referring care providers to be aware of the following points.

There are many predictors of maternal cardiovascular complications in pregnant women with CVD. A number of risk stratification tools have been developed from large

populations with a spectrum of CVD such as *Zwangerschap bij Aangeboren Hartafwijkingen (Pregnancy With Congenital Heart Disease) (ZAHARA)*, *Registry Of Pregnancy And Cardiac Disease (ROPAC)*, and *Cardiac Disease in Pregnancy (CARPREG)*.^{2,3,18-20} The CARPREG risk scores were derived and validated within the Canadian population (Fig. 2).^{2,3} The original CARPREG risk score incorporated 4 functional predictors to classify pregnancies as being at low, intermediate, or high risk for maternal cardiovascular complications. The CARPREG II risk score is used to calculate the risk of maternal cardiovascular complications according to functional, lesion-specific, and process of care predictors (Fig. 2).^{3,21} The **modified World Health Organization (mWHO)** risk classification system, was developed using expert consensus to classify maternal cardiac lesions into 5 risk classes corresponding to increasing maternal cardiovascular risk (Supplemental Table S2).²² The CARPREG II risk score has superior predictive accuracy compared with the mWHO risk classification system and the original CARPREG risk score (Fig. 2).²¹

Risk stratification tools should always be supplemented by lesion-specific data and clinical judgement. One approach is to identify pregnancies in women with cardiac lesions associated with high risk of serious maternal cardiovascular complications with high mortality rates (Fig. 3).²¹ In women without high-risk lesions, the CARPREG II risk score can be used to integrate individual patient and lesion characteristics. For those who prefer the mWHO risk classification system, we recommend that general predictors of cardiovascular complications (such as history of previous cardiac events and arrhythmias) be incorporated, which further stratify risk within each mWHO category.

Assisted reproduction technologies can pose additional risks in women with CVD because of ovarian hyperstimulation, thromboembolism, and likelihood of multifetal

	CARPREG II (Points in Brackets)	CARPREG (Points in Brackets)
Functional predictors	<ul style="list-style-type: none"> Cardiac event (heart failure, transient ischemic attack, stroke, or arrhythmia requiring treatment) before current pregnancy* (3) Baseline NYHA III or IV or cyanosis (3) Systemic ventricular ejection fraction < 55% (2) Left heart obstruction (mitral valve area < 2 cm² or aortic valve area < 1.5 cm², or peak left ventricular outflow tract gradient > 30 mm Hg) or at least moderate-severe mitral regurgitation (2) 	<ul style="list-style-type: none"> Cardiac event (heart failure, transient ischemic attack, stroke, or arrhythmia requiring treatment) prior to current pregnancy* (1) Baseline NYHA III or IV or cyanosis (1) Systemic ventricular ejection fraction < 40% (1) Left heart obstruction (mitral valve area < 2 cm² or aortic valve area < 1.5 cm², or peak left ventricular outflow tract gradient > 30 mm Hg) (1)
Lesion specific predictors	<ul style="list-style-type: none"> Mechanical valve (3) Pulmonary hypertension† (2) Coronary artery disease‡ (2) High-risk aortopathy§ (2) 	
Process predictor	<ul style="list-style-type: none"> No prior cardiac interventions (1) Late pregnancy assessment¶ (1) 	
Sum of points and corresponding cardiac risk	<ul style="list-style-type: none"> 0 to 1 point = 5% 2 points = 10% 3 points = 15% 4 points = 22% > 4 points = 41% 	<ul style="list-style-type: none"> 0 point = 5% 1 point = 27% > 1 points = 75%

Figure 2. Maternal cardiovascular risk calculation using the **Cardiac Disease in Pregnancy (CARPREG)** risk scores. NYHA, New York Heart Association functional class. * Excluding events preceding previous cardiac surgery. † Right ventricular systolic pressure ≥ 50 mm Hg in the absence of right ventricular outflow tract obstruction. ‡ Angiographically proven coronary artery obstruction or past myocardial infarction. § Marfan syndrome, bicuspid aortopathy with aortic dimension > 45 mm, Loeys-Dietz syndrome, vascular Ehlers-Danlos syndrome, or previous aortic dissection or pseudoaneurysm. || No previous repair of congenital lesion, valve repair/replacement, or percutaneous/surgical treatment of arrhythmia. ¶ First antenatal assessment > 20 weeks gestation.

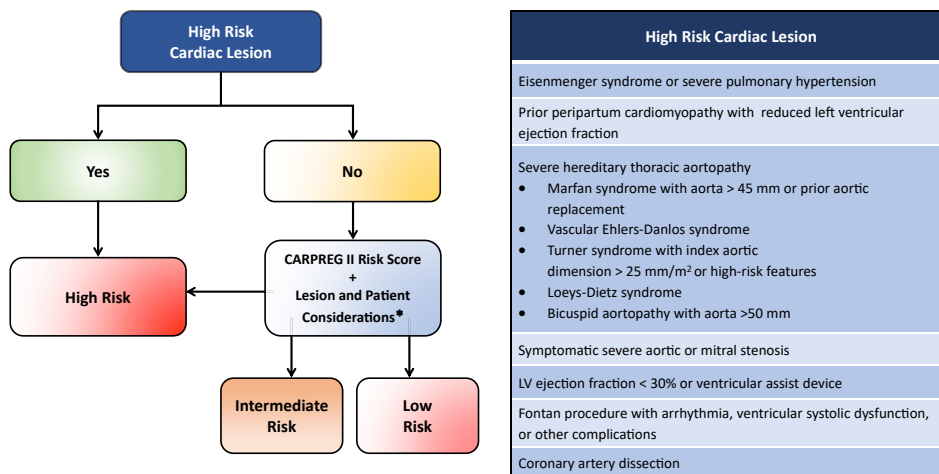


Figure 3. Proposed approach for assessing risk of cardiac complications in pregnant women with heart disease. CARPREG, **C**ardiac **D**isease in **P**regnancy; LV, left ventricular. * Exercise testing, cardiac imaging data, compliance, comorbid conditions, and socioeconomic status and medications including anticoagulants.

pregnancy.¹⁷ Recurrence of CHD and frequency of preterm delivery are further increased.

Although the assessment of obstetric and fetal/neonatal risk is beyond the scope of this article, it is a very important part of the comprehensive risk assessment that should be provided in a COP.^{17,21}

When counselling takes place before conception, there are opportunities to better define and mitigate risk by: (1) cardiac

testing to define cardiac lesion and functional capacity; (2) stopping medications contraindicated in pregnancy and ascertaining clinical stability without these medications; (3) interventions to reduce risk (ie, smoking cessation, intervention for severe aortic stenosis [AS] or mitral stenosis [MS]); and (4) offering genetic counselling if appropriate.^{17,23} Regardless of when the counselling occurs, the following areas need to be discussed and recommendations provided:



Data from observational studies are often conflicting regarding the safety of medication in pregnancy and lactation. Therefore, the **risks vs benefits** of treatment should be discussed with the patient on an individual basis. Potential adverse events should be anticipated and screened for (eg, growth restriction).

Drugs that are considered safe	Drugs with limited/conflicting data/use with caution	Drugs that are considered contraindicated	Drugs that are considered contraindicated when breast feeding
Arrhythmia Adenosine, Bisoprolol, Digoxin*, Lidocaine, Metoprolol, Nadolol, Propranolol	Arrhythmia Diltiazem, Flecainide, Procainamide, Propafenone, Sotalol, Verapamil	Arrhythmia Amiodarone**, Atenolol, Ivabradine	Arrhythmia Amiodarone, Ivabradine
Hypertension/Heart failure Labetalol, Methyl-dopa, Metoprolol, Nifedipine, Bumetanide, Carvedilol, Furosemide, Dobutamine, Dopamine, Norepinephrine	Hypertension/Heart failure Amlodipine, Hydralazine, Nitrates, Nitroprusside, Hydrochlorothiazide, Metolozone, Milrinone, Torsemide	Hypertension/Heart failure ACE-inhibitors, Aldosterone antagonists, ARBs, ARNi, SGLT-2 inhibitors	Hypertension/Heart failure ACE-inhibitors other than Captopril, Lisinopril or Enalapril, Aldosterone antagonists, ARBs, ARNi, SGLT-2 inhibitors
Anticoagulation/Antiplatelets/Thrombolytics Aspirin, Low molecular weight heparin, Unfractionated heparin	Anticoagulation/Antiplatelets/Thrombolytics Clopidogrel, Ticagrelor, Warfarin, Argatroban, Bivalirudin, Fondaparinux, Alteplase, Streptokinase, Tenecteplase	Anticoagulation/Antiplatelets/Thrombolytics Direct oral anticoagulants	Anticoagulation/Antiplatelets/Thrombolytics Direct oral anticoagulants
	Pulmonary Hypertension/Others Epoprostenol, Iloprost, Sildenafil, Treprostinil	Pulmonary Hypertension/Others Bosentan and other ERAs, Statins	Pulmonary Hypertension/Others Statins, Bosentan & other ERAs

*Digoxin serum levels are unreliable during pregnancy. ** May be used if other therapies have failed.

Figure 4. Cardiac medications safety in pregnancy and breastfeeding.^{23,24} ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; ARNi, angiotensin receptor neprilysin inhibitor; ERA, endothelin receptor antagonist; SGLT-2, sodium-glucose cotransporter-2.

- (A) Cardiovascular medications: Figure 4 shows cardiac medications that can be used during pregnancy and those that are contraindicated during pregnancy and/or lactation.^{23,24}
- (B) Site and type of pregnancy care: The optimal plan for follow-up, investigations, and delivery is determined in the COP, which takes into account cardiac/noncardiac risk and the woman's home community with the following options: (1) exclusive care in a COP (recommended for moderate- to high-risk pregnancies); (2) shared care between a COP and local obstetric care, after initial evaluation in a COP (possible for moderate-risk pregnancies provided there is sufficient local cardiac and obstetric expertise); and (3) initial review in a COP, no regular cardiology care during pregnancy, and local obstetric care (recommended for low-risk pregnancies). Local care can also include community cardiology and midwifery in addition to obstetrics.
- (C) Fetal echocardiogram when there is increased risk of CHD in the fetus determined by the presence of CHD in either the mother or father. A fetal echocardiogram is performed at 20 weeks' gestation and is in addition to the routine anatomic ultrasound examination.
- (D) Management during labor and delivery: Vaginal delivery is recommended in most instances, with cesarean delivery reserved for specific cardiac conditions and circumstances including: (1) a woman who presents in labor while receiving vitamin K antagonists or having been receiving one in the preceding 2 weeks; (2) severe PHT; (3) severely decompensated woman in whom delivery needs to be achieved quickly; and (4) aggressive aortic pathology. Induction at term is considered for high-risk pregnancies, for women receiving heparin or who have to relocate to their site of delivery. Invasive hemodynamic monitoring is seldom indicated but may be used in select situations in which the hemodynamic data are required to guide management. In women with intracardiac shunts, air and particulate filters in intravenous lines might help prevent embolism. For patients who are at moderate to high risk, a multidisciplinary meeting should be convened in the antepartum period to develop and document a labor and delivery plan.

Valvular Heart Disease

Native and acquired valvular disease remain important causes of maternal morbidity and mortality. Women with a mechanical valve are at especially high risk for complications in pregnancy.²⁵ Care providers should be aware of red flags indicative of women at particularly high risk of complications (Fig. 5).²⁵

Native valve disease

Stenotic lesions. Women with stenotic valve lesions are at risk for cardiac complications during pregnancy because of the inability of the heart to accommodate the increase in cardiac output across the fixed valve orifice. Common cardiovascular complications include arrhythmias and HF, and in general, can be treated medically.

Percutaneous balloon valvuloplasty (PBV) as a bridge to surgery or as a therapeutic option for stenotic valvular disease should be considered during a patient's pregnancy when pharmacologic therapy is ineffective for those with severe congenital aortic stenosis (AS) or rheumatic MS with less than moderate concurrent regurgitation. PBV using fluoroscopic guidance should ideally be performed after 15 weeks' gestation and the completion of organogenesis. PBV may be performed using transesophageal echocardiography guidance to reduce or obviate the need for ionizing radiation.²⁶

Mitral stenosis. The severity of MS determined pre-pregnancy using standard criteria determines the risk of decompensation. Pregnant women with severe MS have a 3% mortality risk, 37% risk of developing pulmonary edema, and a 16% risk of developing new or recurrent arrhythmias.²⁷ In contrast, pregnant women with moderate MS might experience the same complications in 1%, 18%, and 5%, respectively. Women with severe MS should be counselled about the potential significant complications to mother and fetus and should be evaluated for a valvular intervention before pregnancy.^{28,29} If already pregnant, women with severe MS can be offered the option of early pregnancy termination.

Pregnant women with MS are at risk for atrial arrhythmias and this can be associated with thromboembolic complications.^{2,27,29} Women with MS and atrial fibrillation or a previous thromboembolic episode should be anticoagulated. Anticoagulation can also be considered in women with no documented atrial fibrillation but who have moderate or greater MS with spontaneous echo contrast in the left atrium, a large left atrium (≥ 60 cc/m²), or HF. In women with HF, rate-slowing medications (ie, β -blockers) will slow the heart rate, extend diastolic filling time, reduce the transmitral gradients, and decrease the left atrial pressure and pulmonary venous congestion. Diuretics can also be used to treat HF refractory to adequate rate control.

Aortic valve stenosis. Pregnancy is usually well tolerated in women with asymptomatic mild to moderate AS. An exercise test might help to risk-stratify women by eliciting symptoms, arrhythmias with exertion, and assessment of exercise tolerance and blood pressure response to exercise. Women with moderate to severe asymptomatic AS should be monitored carefully for the development of symptoms (angina, arrhythmias, syncope, HF) during pregnancy. As a result of appropriate medical attention and management, maternal mortality is no longer common.^{28,30,31} In a recent meta-analysis, the risks of death, pulmonary edema, and new or recurrent arrhythmias were 2%, 9%, and 4%, respectively, in pregnant women with severe AS and 0%, 8%, and 2%, respectively, in pregnant women with moderate AS.²⁷

Women with severe AS who develop HF should be treated with diuresis. If women remain symptomatic or have HF despite medical therapy, consideration should be given to relief of the AS either with a PBV or surgical aortic valve replacement. In select cases, transcatheter aortic valve implantation might be an option.

Regurgitant lesions. Aortic and pulmonary regurgitant lesions are usually well tolerated during pregnancy.³² However, moderate to severe atrioventricular regurgitant lesions are

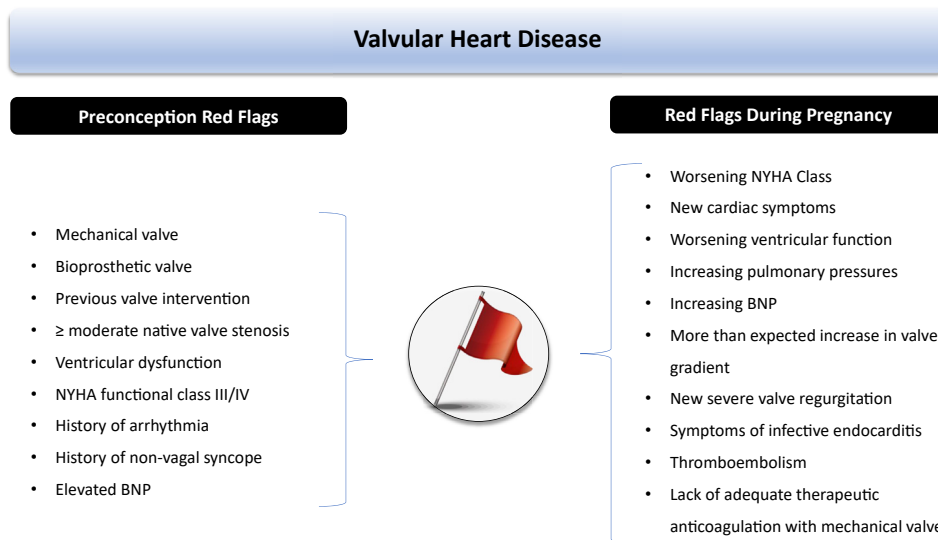


Figure 5. Preconception and pregnancy red flags: valvular heart disease. BNP, brain natriuretic peptide; NYHA, New York Heart Association.

associated with a 15% rate of adverse outcomes including HF and arrhythmias, particularly in the setting of ventricular dysfunction and PHT.³² In those with moderate to severe rheumatic mitral regurgitation, HF can occur in 20%-25% of patients.³³ This can be managed medically in most cases with diuretics and afterload reduction.

Prosthetic valves and anticoagulation

The advantages and disadvantages of the various prosthetic valves (bioprosthetic, mechanical, homografts) should be discussed in detail before choosing a valve for a woman of childbearing age.³⁴ The choice of valve dictates the care required through a pregnancy, most importantly the requirement for anticoagulation. Pregnancy in women with a

mechanical valve is high risk and they should be counselled about the potential significant complications to mother and fetus. During pregnancy, these women require regular clinical and echocardiographic follow-up.

Anticoagulation for women with a mechanical valve may be achieved with warfarin, low molecular weight heparin, or full-dose unfractionated heparin. There are multiple anticoagulation regimens, which require meticulous attention to detail, which should be managed within a COP in conjunction with hematology expertise.³⁵ There is no ideal anticoagulant for pregnant women with mechanical valves because there are varying maternal and fetal risks associated with the different types of anticoagulation strategies (Fig. 6).³⁵ Warfarin is associated with the lowest risk of valve thrombosis but crosses the placenta and poses the highest risk of miscarriage, fetal embryopathy, fetopathy, and fetal death. These risks are highest if warfarin is taken in the first trimester and/or warfarin dose exceeds 5 mg daily, although some fetal risk remains with use in the second to third trimesters. Heparin does not cross the placenta and is therefore not associated with fetal risk, however, the rates of maternal valve thrombosis and maternal mortality are higher than with warfarin particularly when heparin is not appropriately dosed and monitored. With all of this in mind, there are 3 potential strategies: (1) warfarin throughout pregnancy, particularly if the required dose is < 5 mg daily; (2) heparin throughout pregnancy; and (3) sequential therapy, with heparin during the first trimester and warfarin during the second and third trimesters.

The risk of mechanical valve thrombosis was 4.7% in the ROPAC and this was associated with a 20% mortality.²⁵ In a recent meta-analysis, the risk of a thromboembolic complication with a mechanical valve was 3%-9%, dependent on the anticoagulation regimen.³⁶ Valve thrombosis can be a serious complication resulting in maternal morbidity and mortality as well as fetal loss. If valve thrombosis is suspected, emergent transfer to a COP cardiac surgical center should be undertaken.

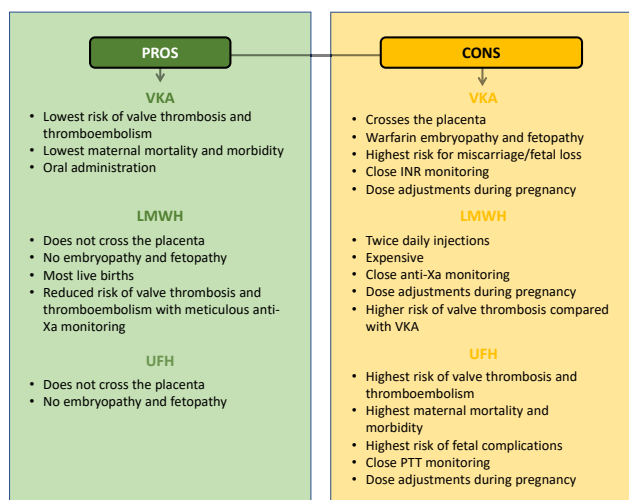


Figure 6. Pros and cons of anticoagulation strategies in pregnancy. INR, international normalized ratio; LMWH, low molecular weight heparin; PTT, partial thromboplastin time; UFH, unfractionated heparin; VKA, vitamin K antagonist.

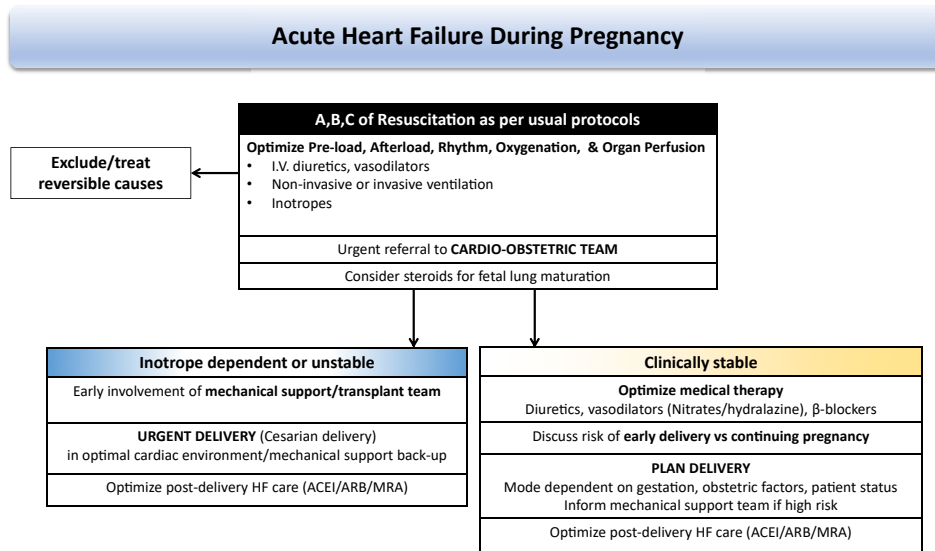


Figure 7. Management of acute heart failure during pregnancy. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; HF, heart failure; I.V., intravenous; MRA, mineralocorticoid receptor antagonist.

Cardiomyopathy

Cardiomyopathy and other myocardial diseases are common cardiac causes of maternal morbidity and mortality. In women with a known cardiomyopathy, a major component of pre-conception counselling involves reviewing regular medications because many standard HF therapies are contraindicated in pregnancy (angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, angiotensin receptor neprilysin inhibitors, mineralocorticoid receptor antagonists, ivabradine, and sodium-glucose cotransporter-2 (SGLT2) inhibitors (Fig. 4). Assessing left ventricular (LV) function without such medications improves risk stratification before pregnancy. Diuretics and β -blockers should be continued and hydralazine and nitrates are alternatives to the contraindicated medications. If pregnancy occurs with use of usual HF medication,

contraindicated medications should be discontinued as soon as possible. Tracking echocardiographic parameters and brain natriuretic peptide serially during pregnancy helps direct proactive care. Similarly, all women post heart transplantation require close review before pregnancy, including review of immunosuppressant medications, and follow-up through pregnancy at a COP.

Acute HF

Effort intolerance, fatigue, and ankle edema are common findings during normal pregnancy and therefore similar signs and symptoms of HF can be missed. Suspicion should be high with new onset of “asthma,” persisting sinus tachycardia, orthopnea, and paroxysmal nocturnal dyspnea. HF

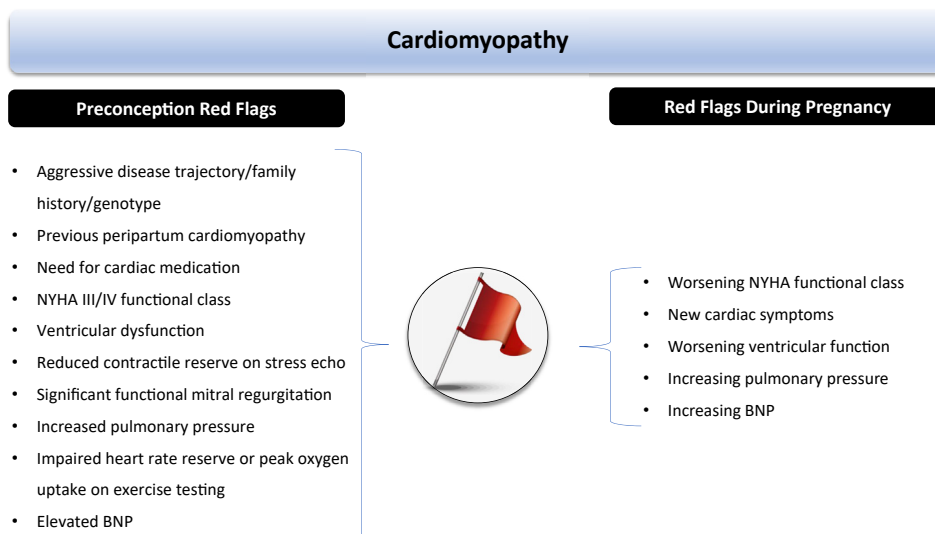


Figure 8. Preconception and pregnancy red flags: cardiomyopathy. BNP, brain natriuretic peptide; NYHA, New York Heart Association.

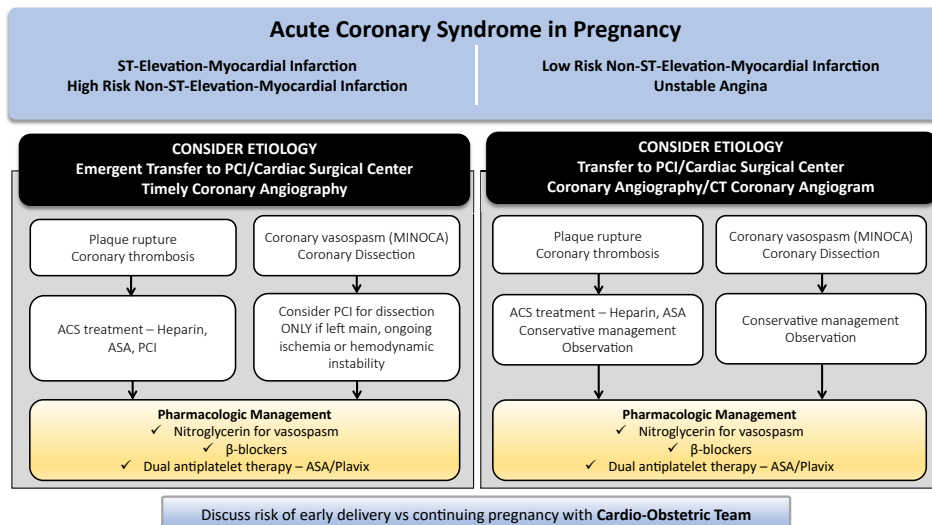


Figure 9. Management of ACS during pregnancy. ACS, acute coronary syndrome; ASA, acetylsalicylic acid; CT, computed tomography; MINOCA, myocardial infarction in the absence of coronary artery disease; PCI, percutaneous coronary intervention.

presentation during pregnancy occurs generally in the second or third trimester or in the postpartum period.²⁰ The assessment and treatment of acute HF follow the same principles as for the nonpregnant patient (Fig. 7). Care providers should be aware of red flags indicative of women particularly at higher risk of complications (Fig. 8).

Peripartum cardiomyopathy. PPCM is an idiopathic condition with LV systolic dysfunction (ejection fraction [EF] < 45%) occurring toward the end of pregnancy or within 5 months after delivery, when no other cause is found. When assessing the patient, it is important to take a comprehensive family history because genetic forms of dilated cardiomyopathy might be unmasked and present similarly. The risk factors for developing PPCM include African ethnicity, maternal age, smoking, diabetes, preeclampsia, and multiparity. There has been research interest in the use of bromocriptine, a prolactin inhibitor, to treat PPCM but this remains an unproven therapy.³⁷ Despite the possible association between prolactin and PPCM, there is no strong evidence at present to recommend avoiding breastfeeding.

Women with known preexisting cardiomyopathy

Dilated cardiomyopathy. Dilated cardiomyopathy of any etiology might present before or during pregnancy. Predictors of cardiovascular complications including mortality are an EF < 40% and/or New York Heart Association functional classification of III-IV.³⁸ Pregnancy in women with severe LV systolic dysfunction (EF < 30%) is very high risk and counselling about the potential significant complications to mother and fetus should occur.³⁸ If already pregnant, early termination should be offered. In patients with familial or genetic forms of cardiomyopathy, a full genetic assessment should be performed before pregnancy.

Previous PPCM. Patients with previous PPCM and normalization of LV function with good contractile reserve on stress echocardiography can consider future pregnancy after thorough risk stratification and understanding that there is a risk of recurrent PPCM.³⁷ However, persisting LV dysfunction predisposes women to recurrent HF, ventricular dysfunction, and even death in up to 25% and pregnancy should be discouraged.³⁷

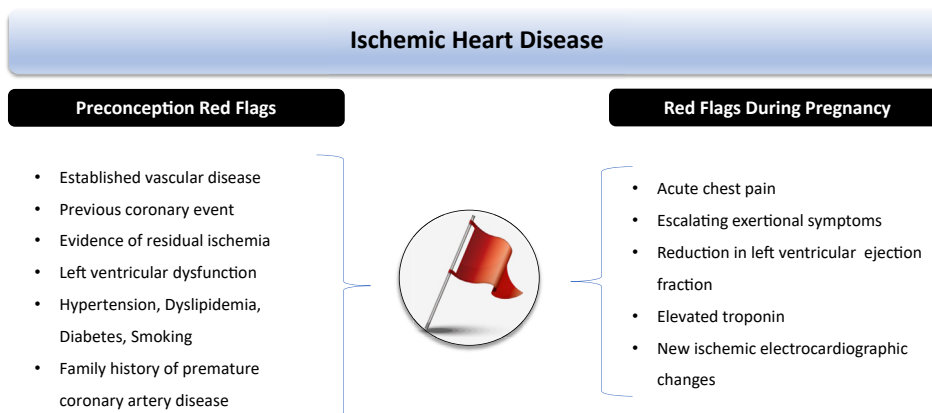


Figure 10. Preconception and pregnancy red flags: ischemic heart disease.

After an episode of PPCM, expert counselling should be routinely offered regarding recurrence risk in a future pregnancy.

Hypertrophic cardiomyopathy. Most patients with familial hypertrophic cardiomyopathy do well during pregnancy. Exceptions are women with prepregnancy symptoms despite optimal medical treatment, moderate or greater LV dysfunction, diastolic dysfunction, PHT, and/or severe LV outflow tract obstruction.³⁹ β -Blockers and diuretics might be of benefit particularly in women with symptoms related to systolic or diastolic dysfunction.

Ischemic Heart Disease

Pregnancy is associated with a three- to fourfold increase in acute coronary syndrome (ACS) risk compared with age-matched nonpregnant women. It is most commonly related to coronary atherosclerotic plaque rupture, dissection, or myocardial infarction in the absence of coronary artery disease (thrombosis, vasospasm, microvascular dysfunction).^{40,41} Incidence of ACS ranges between 3 and 8 cases per 100,000 deliveries with mortality upward of 7%.^{42,43} Presentation is typically in the third trimester and postpartum periods, and management is dependent on the clinical presentation and underlying cause, which is best determined using coronary angiography (Fig. 9).^{40,41}

Atherosclerosis/thrombosis

Acute ST-segment elevation myocardial infarction (STEMI) or high-risk non-STEMI due to plaque rupture or thrombosis requires a timely invasive strategy (Fig. 9). In the case that percutaneous coronary intervention (PCI) is not readily available, women should be safely transferred to a site with PCI capabilities. Thrombolysis can be considered in women with STEMI because it does not cross the placenta, but it is not a preferred option because coronary dissection is a leading cause of myocardial infarction in pregnant women, and should not be treated with thrombolysis.⁴⁴ Low-risk ACS should be managed conservatively. Women with preexisting coronary atherosclerosis have a 10% risk of experiencing an ischemic event in pregnancy, are considered high risk, and should continue low-dose aspirin and β -blocker therapy through pregnancy.⁴⁵ Care providers should be aware of red flags indicative of women particularly at higher risk of complications (Fig. 10).

Pregnancy-associated spontaneous coronary artery dissection

ACS presentation due to pregnancy-associated spontaneous coronary artery dissection (p-SCAD) is commonly associated with left main, left anterior descending, or multi-vessel involvement and thus is associated with ventricular dysfunction and life-threatening maternal complications.⁴⁶ There must be a high clinical suspicion of p-SCAD because localized dissections can be missed. Conservative management with monitoring in-hospital is preferred, with lesion healing expected to occur over months.⁴⁶ Pharmacologic management consists of β -blockers and antiplatelet therapy. PCI can propagate the dissection and should only be considered if high-risk features are present.⁴⁶ Because there is a risk of recurrence of p-SCAD, repeat pregnancy is high risk and

women should be counselled about the potential significant complications to mother and fetus.

Arrhythmias in Pregnancy

Many different arrhythmias can present in pregnancy and care providers should be aware of red flags indicative of women at higher risk of complications (Fig. 11). Consultation with an electrophysiologist within a COP can be considered.

Supraventricular arrhythmia

Up to 0.5% of pregnancies will be complicated by supraventricular tachycardia (SVT).⁴⁵ The first presentation of SVT during pregnancy is not uncommon.⁴⁷ The most common SVTs in pregnancy are atrioventricular nodal reentry and atrioventricular reentrant tachycardia; Figures 12 and 13 show an outline of management strategies. Wolff-Parkinson-White syndrome with an accessory pathway can be associated with a worsening arrhythmia burden in pregnancy. Supraventricular arrhythmias occur in up to 15% of patients with structural heart disease during pregnancy, and in many cases the hemodynamic changes exacerbate arrhythmia in a previously stable patient. Risk factors include preexisting arrhythmia, mitral valve disease, β -blocker use before pregnancy, and left-sided structural lesions.⁴⁸

Atrial fibrillation or flutter is most commonly seen in women with structural heart disease and there are various therapeutic options to consider including cardioversion (Fig. 14). There is little consensus regarding thromboprophylaxis for atrial fibrillation or flutter in pregnancy in the absence of structural heart disease.⁴⁹ Anticoagulation should be initiated if atrial flutter or fibrillation or intra-atrial reentrant tachycardia is documented in any pregnant woman with structural heart disease. Although established risk scoring systems have not been validated for use in pregnancy, anticoagulation should be initiated with a Congestive Heart Failure, Hypertension, Age \geq 75, Diabetes, and Prior Stroke/Transient Ischemic Attack (doubled) (CHADS₂) risk factor score \geq 1 in the absence of structural heart disease.¹⁰

Ventricular arrhythmias

Ventricular arrhythmias (VAs) range from asymptomatic isolated premature ventricular beats to nonsustained ventricular tachycardia or sustained VAs resulting in syncope or sudden cardiac death. Sustained VAs are more common in women with structural heart disease.^{47,48} Overall, 27% of women with a history of VA will have a recurrence in pregnancy,⁴⁸ with increased risk of adverse neonatal outcomes.⁴⁸ Assessment should include screening for inherited arrhythmia disorders or cardiomyopathy. PPCM must be considered when VAs complicate the last several weeks of pregnancy or early postpartum period.¹⁰

Established guidelines for the acute and long-term management of VAs should be followed, but consultation with an arrhythmia specialist is recommended (Fig. 15). Catheter ablation should be considered for significant VAs detected before pregnancy.⁵⁰ Alternatively, medical stabilization, followed by catheter ablation post partum can be considered. Catheter ablation can be considered during pregnancy in cases of refractory arrhythmia in a centre with experienced

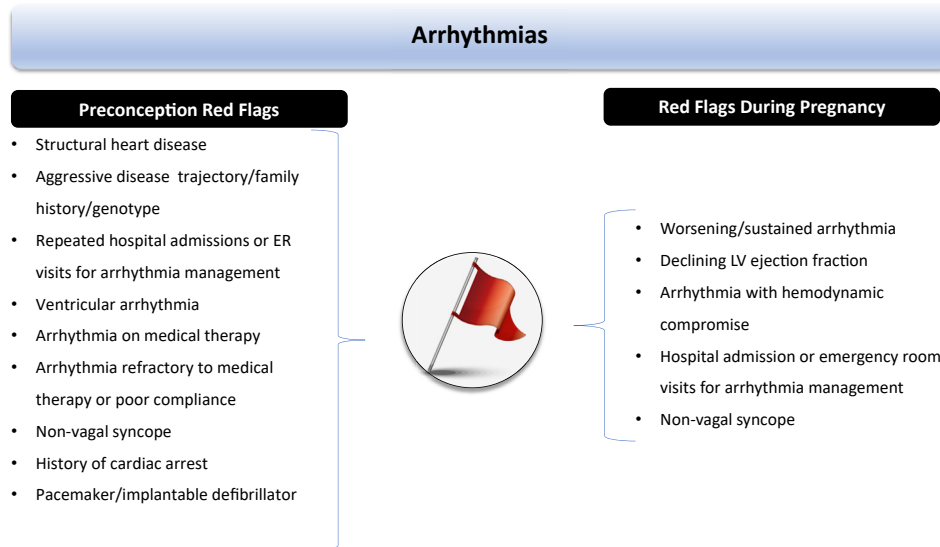


Figure 11. Preconception and pregnancy red flags: arrhythmias. ER, emergency room; LV, left ventricular.

operators, with a nonfluoroscopic approach if available. Lead shielding can reduce the dose of radiation to the fetus but does not eliminate exposure. Although cardiac arrest is rare in pregnancy, emergent cesarean delivery for fetal rescue is indicated if there is no return of spontaneous circulation after 4 minutes of resuscitation. Emergent cesarean delivery might also be performed as a part of the maternal resuscitation.⁵¹ Other resuscitation considerations include, ideally obtaining intravenous access above the diaphragm, early advanced airway management including difficult airway anticipation, and manual left uterine displacement.

Device considerations

Detailed guidelines governing implantable cardioverter-defibrillator (ICD) implantation have been published and are not altered by pregnancy. Women with a pacemaker or an ICD

should be evaluated before pregnancy and at least once during pregnancy to determine dependency on pacing as well as basic device settings and system integrity. When using monopolar electrosurgery, the current path should be directed away from the device and the duration of bursts limited to avoid pacing inhibition or inappropriate ICD therapy. A magnet should always be immediately available in the delivery room.

Aortic Disease

Pregnancy among women with heritable thoracic aortic disease (HTAD) is associated with increased maternal cardiovascular risk, dependent specifically on the underlying HTAD type and associated red flags (Fig. 16). There is an increased risk of progressive aortic dilation and dissection due to associated hemodynamic and hormonal changes.⁵² Although uncommon, when

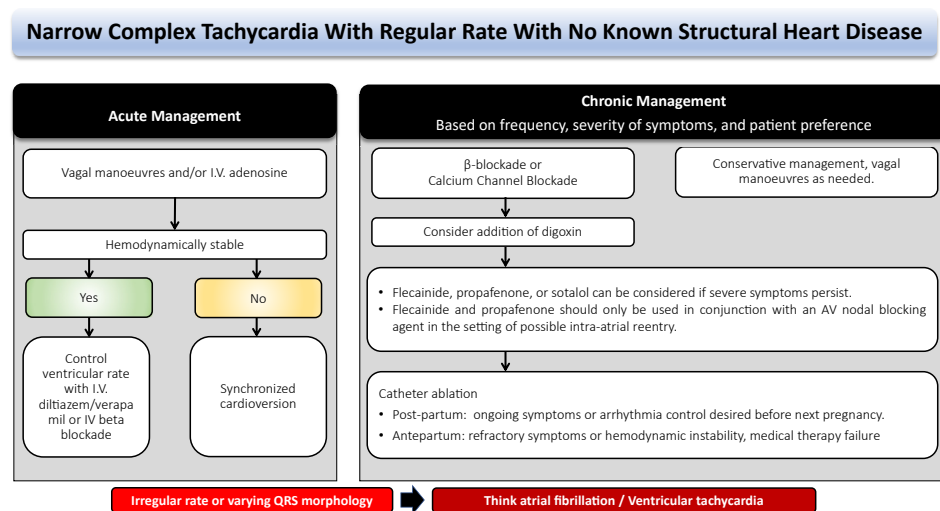


Figure 12. Management of narrow complex tachycardia with no known structural heart disease during pregnancy. AV, atrioventricular; I.V., intravenous.

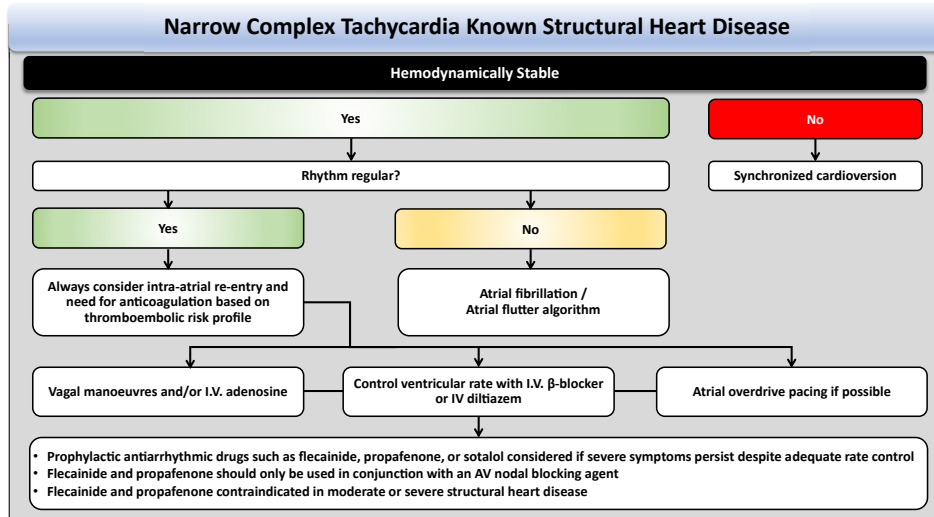


Figure 13. Management of narrow complex tachycardia with known structural heart disease during pregnancy. AV, atrioventricular; I.V., intravenous.

aortic dissection occurs, it is associated with 30% maternal mortality.⁵² Therefore, it is imperative that women with HTAD be identified before conception, have imaging of the entire aorta and branch vessels, gene panel testing when applicable, and receive accurate counselling around aortic dissection risk. Genetic counselling to discuss the results and implications of gene testing and options around preimplantation genetic diagnosis is important. Critical to this is making a definitive diagnosis of the cause of the aortopathy before pregnancy whenever possible because it affects risk assessment and delivery of care through pregnancy. The need for prophylactic aortic root surgery for the prevention of aortic dissection should be considered before pregnancy. Other coexistent cardiac issues should also be evaluated and warrant attention.

Bicuspid aortic valve

Ascending aortic dilation can occur in the absence of valve dysfunction, and is present in up to 50% of patients. The rate of dissection is low at approximately 0.03% outside of pregnancy and likely increases to a small degree in pregnancy specifically among women with a dilated aorta.⁵³ However, bicuspid aortic valve accounts for only a small percentage of dissections in pregnancy and is a more benign aortopathy compared with other HTADs.⁵⁴ Prophylactic aortic surgery to facilitate safe pregnancy should be considered at an ascending aortic diameter ≥ 50 mm.

Marfan syndrome

Overall risk of dissection in pregnancy is increased at approximately 3%, although the risk in women with an aortic

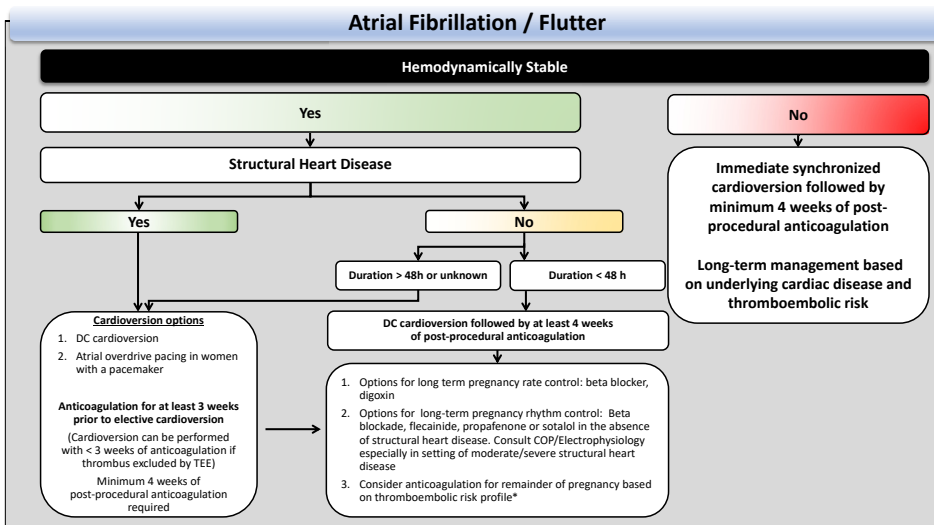


Figure 14. Management of atrial fibrillation/flutter during pregnancy. *Anticoagulation should be initiated in the presence of structural heart disease and/or CHADS₂ risk score ≥ 1 . COP, cardio-obstetric program; TEE, transesophageal echocardiography.

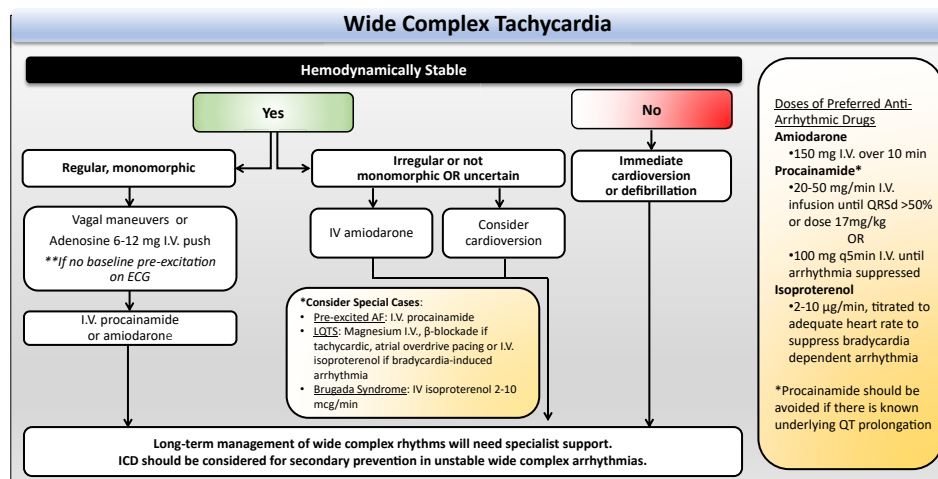


Figure 15. Management of wide complex tachycardia during pregnancy. AF, atrial fibrillation; ECG, electrocardiogram; I.V., intravenous; LQTS, long QT syndrome; q5min, every 5 minutes; QRSd, QRS duration.

root < 40 mm is approximately 1%.⁵⁵ The risk of dissection can be as high as 10% in women with aortic root diameter > 40 mm, rapid dilatation of aorta, or history of dissection.⁵² Pregnancy should be avoided in the setting of an ascending aortic diameter ≥ 45 mm and prophylactic aortic surgery should be considered, however the risk of type B dissection remains. In the setting of intermediate aortic dimensions of 40-45 mm, other factors such as family history of dissection and rate of aortic growth help to inform the risk of moving forward with a pregnancy.

Vascular Ehlers-Danlos syndrome

This is a severe connective tissue disorder characterized by frail vascular tissue. Vascular and/or organ rupture during pregnancy has been reported to be as high as 50% and mortality reported to be approximately 6%.⁵⁶ Pregnancy is therefore very high risk and women should be counselled about the potential significant complications to mother and fetus.

Turner syndrome

The risk of aortic dissection in pregnancy has been reported to be approximately 1%-2%, on the basis of extrapolation from retrospective data.^{57,58} More recent multicentre data would suggest that risk is lower among women without structural heart disease.⁵⁹ As such, we can expect to see more pregnancies in Turner syndrome patients with a structurally normal heart and/or mosaicism.⁵⁹ Pregnancy has been thought to be higher risk among those with aortic size indexed of 2.5 cm/m² or aortic size index of 2.0 cm/m² with at least 1 of hypertension, bicuspid aortic valve, aortic coarctation, or transverse arch elongation and requires close surveillance.

Loeys-Dietz syndrome

Loeys-Dietz syndrome results in widespread medium or large vessel vascular disease and its natural history is more aggressive with increased rates of vascular and uterine rupture compared with Marfan syndrome. Although recent data

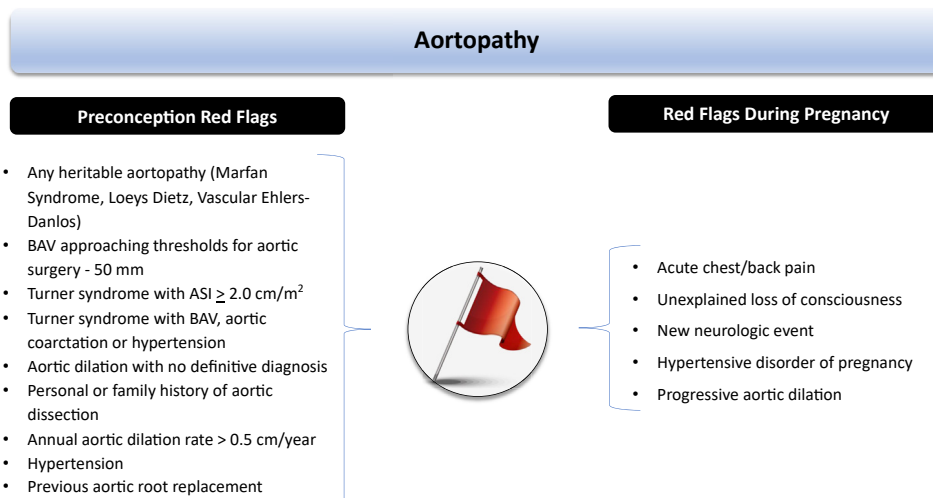


Figure 16. Preconception and pregnancy red flags: aortopathy. ASI, aortic size indexed; BAV, bicuspid aortic valve.

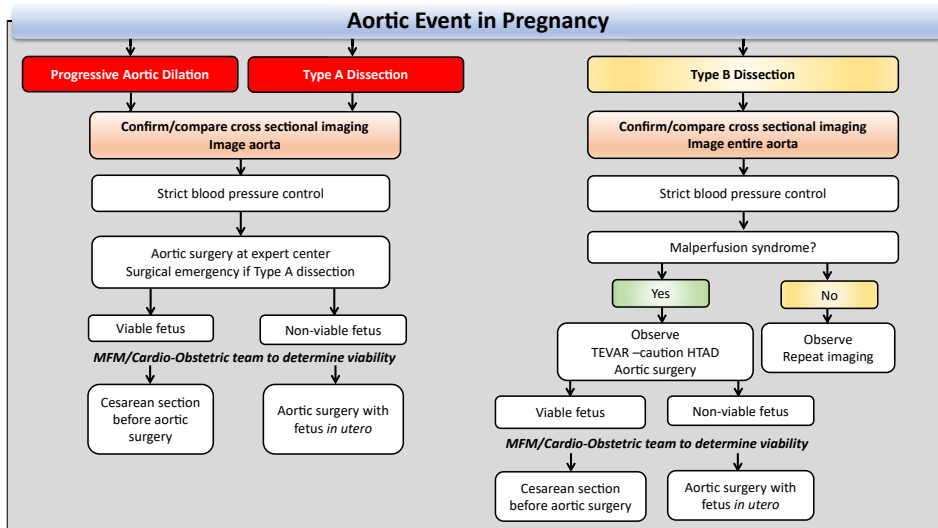
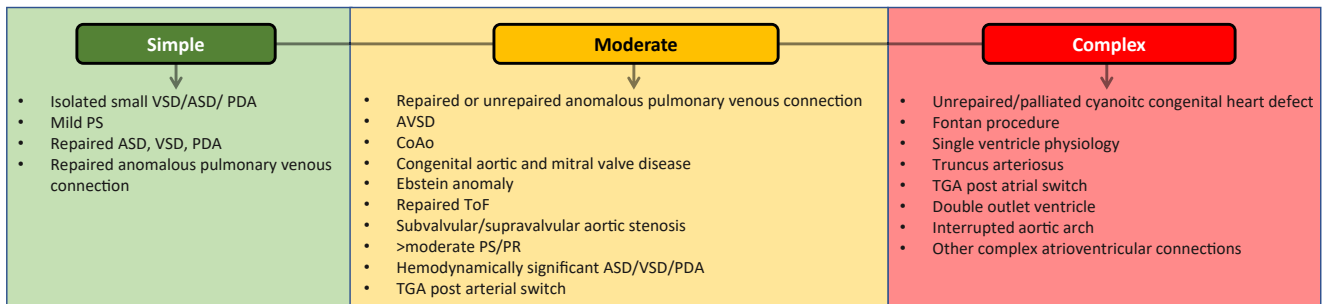


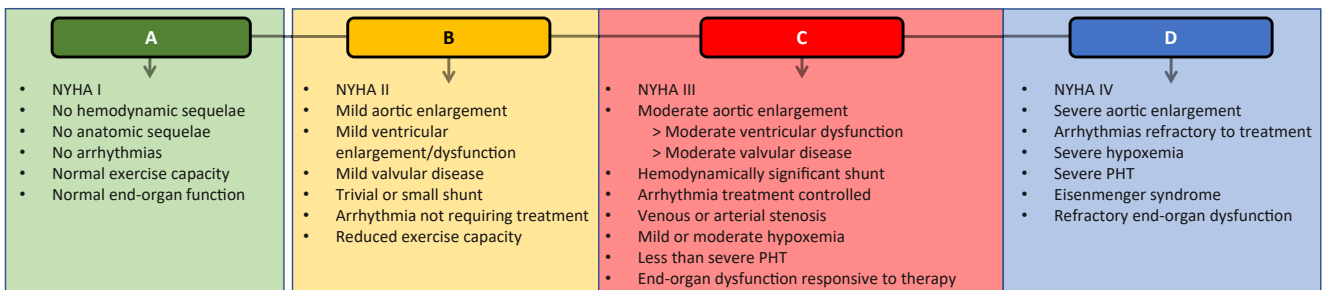
Figure 17. Management of an aortic event in pregnancy. HTAD, heritable thoracic aortic disease; MFM, Maternal-Fetal Medicine; TEVAR, thoracic endovascular aortic repair.

suggest more favourable outcomes than previously thought, pregnancy is still high risk and cannot be considered safe at any aortic dimension.⁶⁰ Pregnancy is contraindicated in the setting of an ascending aortic diameter ≥ 45 mm and prophylactic aortic surgery should be considered, however, the risk of type B

dissection remains. The literature is evolving and this particular scenario is an example of the critical role that a COP can play in counselling and guide decision-making. In this case factors such as family history of dissection and rate of aortic growth help to inform the risk of moving forward with a pregnancy.



Low- to High-Risk Anatomical Complexity in a Woman With Congenital Heart Disease



Low- to High-Risk Physiological Stage in a Woman With Congenital Heart Disease

Figure 18. Anatomic and physiologic risk classification of congenital heart disease in pregnancy. Adapted from the classification system outlined in Stout et al.⁶³ ASD, atrial septal defect; AVSD, atrio-ventricular septal defect; CoAo, coarctation of the aorta; NYHA, New York Heart Association; PDA, patent ductus arteriosus; PHT, pulmonary hypertension; PR, pulmonic regurgitation; PS, pulmonic stenosis; TGA, transposition of the great arteries; ToF, tetralogy of Fallot; VSD, ventricular septal defect.

Follow-up through pregnancy will depend on the underlying aortopathy and associated red flags. Regular echocardiographic assessment of the aorta should occur every 4–12 weeks during pregnancy and at 3 and 6 months post partum. Women with known distal aortic dilation should undergo magnetic resonance imaging (MRI) in pregnancy to assess stability. Similarly, women with HTAD who present in pregnancy without comprehensive imaging of the entire aorta before pregnancy should undergo MRI. Noncontrast MRI is thought to be safe in pregnancy but is generally avoided in the first trimester. In general, it is advised to avoid the use of gadolinium-based contrast agents during pregnancy. Medical therapy for HTAD has been adopted from Marfan data, and β -blockers remain the treatment of choice to reduce aortic wall shear stress and growth rate.^{61,62} Strict blood pressure control is important to reduce risk of aortic dissection. Aortic dissection occurs most commonly in the third trimester or early postpartum period, and chest pain should lead to rapid assessment for aortic dissection (Fig. 17). The preferred diagnostic modality would be computed tomography imaging of the aorta; it is rapid, does not require sedation, and can clearly define the extent of aortic dissection. Most dissections involve the ascending aorta (type A), but dissections in the descending aorta can also occur (type B). Previous aortic root replacement does not preclude a woman from having a type B dissection in pregnancy. Normal aortic dimensions in patients with HTAD also do not preclude a woman from having a dissection.

Congenital Heart Disease

Just under 1% of the population have CHD and advances in surgery and cardiology result in most women born with moderate to severely complex disease now reaching child-bearing age.¹⁵ CHD accounts for most patients managed in a COP. The wide spectrum of lesions and repairs necessitates their inclusion within such a clinic with a cardiologist who has expertise in adult CHD and obstetric cardiology.

In the past, severity of disease was classified according to anatomy but recent guidelines have acknowledged that the severity of disease and therefore pregnancy risk is determined by a combination of native anatomy, surgical repair, and current physiologic status (Fig. 18).⁶³ For example, a woman with a simple uncomplicated atrial septal defect will have a very low risk of complications whereas a woman with a similar-sized atrial septal defect with associated PHT will be at significant risk of complications. We therefore recommend that all women with CHD undergo evaluation and risk stratification by a COP-based adult CHD specialist. Follow-up through pregnancy will depend on their risk secondary to native anatomy, surgical repair, and physiologic status.

Pulmonary Hypertension

For a detailed outline of the causes and definitions of PHT the reader is referred to the recent Canadian Cardiovascular Society position statement.⁶⁴ Maternal cardiovascular risk in pregnancy depends on the etiology of the PHT. Advances in therapies for group 1 pulmonary arterial hypertension have helped to improve maternal cardiovascular outcomes. However, maternal cardiovascular risk remains high and women

with significant pulmonary arterial hypertension should be counselled about the potential significant complications to mother and fetus.⁶⁵ We strongly recommend that all women with PHT need careful preconception assessment to determine pregnancy risk and identify any interventions or therapies that mitigate that risk. If pregnancy is pursued then close surveillance within a COP in collaboration with PH experts is essential.

Conclusion

Cardio-obstetrics is an emerging field. Cardiologists should be aware that pregnancy is a cardiovascular stress and that women of childbearing age with CVD should have preconception counselling within a COP. These programs offer comprehensive multidisciplinary pregnancy care. Canadian COPs have been established at most major Canadian centres. There is also growing recognition that cardiology and obstetric trainees should have exposure to this field of cardiology.

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Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at <https://doi.org/10.1016/j.cjca.2021.06.021>.