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Cardio-Obstetrics Part 3: Acquired Cardiovascular Disorders: JACC Focus Seminar

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Abstract

Acquired cardiovascular conditions are a leading cause of maternal morbidity and mortality. A growing number of pregnant women have acquired and heritable cardiovascular conditions and cardiovascular risk factors. As the average age of childbearing women increases, the prevalence of acute coronary syndromes, cardiomyopathy and other cardiovascular complications in pregnancy are also expected to increase. This document, the third of a five-part series, aims to provide practical guidance on the management of such conditions encompassing preconception through acute management and considerations for delivery.

Condensed Abstract

Acquired cardiovascular conditions are a leading cause of maternal morbidity and mortality and the prevalence of acute coronary syndromes, cardiomyopathy and other cardiovascular complications in pregnancy are expected to increase with advancing maternal age. This document, the third of a five-part series, aims to provide practical guidance on the management of such conditions encompassing preconception through acute management and considerations for delivery.

Keywords

cardio-obstetrics; pregnancy; arrythmia; ischemic heart disease; hypertensive disorders of pregnancy

Introduction

Acquired cardiovascular conditions in pregnant women account for the largest proportion of maternal morbidity and mortality, with increasing prevalence (1). Part 3 of this review series will cover cardiovascular conditions predominantly acquired including arrhythmias, cardiomyopathies, hypertensive disorders, and ischemic heart disease. Management of such patients is challenging and requires multidisciplinary discussion among a wide variety of clinicians from maternal fetal medicine to cardiology subspecialties (Central Illustration). This document serves to provide guidance on practical management of these patients from preconception to the peripartum period and beyond.

Arrhythmias

The incidence of arrhythmias during pregnancy is rising and hospitalization for arrhythmia during pregnancy is associated with increased mortality and fetal complications (2). Arrhythmias may develop de novo during pregnancy or pregnancy may exacerbate existing arrhythmias, likely related to hormonal effects. Palpitations during pregnancy are common but do not necessarily correlate with documented arrhythmias on cardiac monitoring.

Preconception Evaluation

Prior history of arrhythmia is the greatest risk factor for arrhythmia during pregnancy (3). Patients should be counseled on risk of recurrence and/or exacerbation of arrhythmia during pregnancy, and of the risks and benefits of potential treatment options, including medications, cardioversion, and ablation. Women who require anticoagulation therapy should be counseled on the potential teratogenicity of warfarin, the lack of safety data for direct oral anticoagulants during pregnancy, and possible need for low molecular weight or unfractionated heparin.

Contraception

Discussion of contraception should occur in a multidisciplinary fashion taking into consideration multiple factors based on the unique risk profile of each woman. Some considerations based on rhythm type and contraceptive type are discussed in Table 1.

General considerations for treatment of arrhythmias in pregnancy

Acute Management of Tachyarrhythmias

Pregnancy should not impede treatment of tachyarrhythmias. Management for the most part should proceed as it would for a non-pregnant patient with unstable rhythm with particular considerations noted in Figure 1. If CPR is required and the uterus is palpable at or above the level of the umbilicus, continuous left uterine displacement should be performed to relieve aortocaval compression (4).

Catheter Ablation

Although catheter ablation is typically avoided during pregnancy, electrophysiological procedures may be performed during pregnancy for arrhythmias refractory to medical therapy with relatively low fetal radiation (5). Contemporary three-dimensional (3-D) mapping systems should be used when possible to minimize fluoroscopy exposure and efforts to reduce necessary radiation exposure such as reduced frame rates should be utilized. Ablation should be performed after the first trimester when possible.

Implantable Devices

The presence of an implantable cardioverter defibrillator (ICD) should not deter women from becoming pregnant unless the underlying cardiac disease is considered a contraindication (6). If an indication arises for ICD placement during pregnancy, implantation is recommended with efforts to reduce fluoroscopy exposure, preferably after the first trimester (7,8). Most patients with bradyarrhythmias who do not require permanent pacemaker (PPM) before delivery can be safely managed during labor without temporary transvenous or transcutaneous pacing.

Medications

In general, optimizing maternal health will yield the best outcome for both mother and fetus; this can be achieved by considering both the efficacy and safety of medication options. Table 2 summarizes anti-arrhythmic drug use in pregnancy and lactation. Although most anti-arrhythmic drugs do not have proven safety data in pregnancy, it is important to weigh the risks and benefits of initiating antiarrhythmic therapy. In general, the presence of hemodynamically significant or sustained arrhythmias would favor initiation of anti-arrhythmic therapy to reduce maternal and fetal risk.

Specific Disorders

Supraventricular Tachycardia (SVT)

It is unclear whether pregnancy itself increases risk for SVT, however 85% of women with prior history of SVT experience worsening of symptoms during pregnancy particularly during the third trimester (9). Presentation of SVT in pregnancy mirrors symptoms in non-pregnant women including sudden onset of palpitations, which may be associated with presyncope, syncope, dyspnea or chest pain.

Atrial fibrillation/atrial flutter

Data are limited regarding the optimal management of atrial fibrillation/flutter during pregnancy which is not specifically addressed in the 2014 AHA/ACC/HRS Guidelines (10). Atrial fibrillation should be treated promptly as pregnancy is a hypercoagulable state, and current thromboembolic risk assessment tools have not been validated in pregnancy. Direct oral anticoagulants have unknown safety profiles during pregnancy; thus heparin or low molecular weight heparin are recommended for anticoagulation (11,12). Warfarin may be considered after the first trimester (12).

Ventricular Arrhythmias

Ventricular tachycardia and ventricular fibrillation are fortunately rare during pregnancy (3). However, pregnancy can exacerbate preexisting ventricular arrhythmias, with recurrent VT occurring in 27% of pregnancies in women with a prior history, particularly in those with structural heart disease (13). Reversible causes of ventricular arrhythmias should be sought and corrected, including electrolyte disturbances, ischemia, and hypoxemia(14).

Bradyarrhythmias

Acute management of bradyarrhythmias should follow standard management resuscitation protocols as performed in non-pregnant patients including considerations for transcutaneous or transvenous pacing.

Congenital Long QT Syndrome

Women with Long QT Syndrome are at increased risk of death as far as out as nine months post-delivery, particularly women with the LQT2 genotype (8,15-17). Treatment with beta-blockers is independently associated with a decrease in the risk for cardiac events (15,17). Beta-blockers should be continued during pregnancy and throughout the postpartum period, including in women who are breastfeeding (7,8).

Syncope

Women with pre-existing postural orthostatic tachycardia syndrome (POTS) may experience unchanged (13-20%), worsened (31-40%), or improved (40-55%) symptoms during pregnancy (18,19). Lifestyle modifications including increased salt and fluid intake, and compression stockings are recommended for the treatment and prevention of symptomatic orthostasis during pregnancy. When severe symptoms refractory to lifestyle modifications persist, medical therapy with propranolol, fludrocortisone, or midodrine may be considered, though data are limited (19). Cardiogenic syncope may occur due to structural heart disease or arrhythmia. Cardiogenic syncope warrant evaluation with electrocardiogram (ECG), echocardiogram, and Holter/event monitoring.

Cardiomyopathies and Heart Failure

Management of heart failure during pregnancy is complex and requires interdisciplinary collaboration across various points of care (Figure 2). Cardiomyopathy associated complications in pregnancy can include heart failure, arrhythmias, or embolic events. For women with significant underlying ventricular dysfunction, symptoms of heart failure may develop as early as the second trimester as plasma volume increases (20). Management of heart failure should include continuation of beta blockade, and diuretics if indicated, and discontinuation of ACE inhibitors/ARBs and mineralocorticoid receptor antagonists. Development of refractory acute heart failure symptoms may prompt consideration of delivery although medical stabilization of the woman is often achievable.

The postpartum period is the highest risk time for the development of clinical heart failure symptoms in women with cardiomyopathy (20,21). While lower extremity edema is common in postpartum women, the presence of jugular venous distension, orthopnea, and

cough are highly suggestive of heart failure. Obtaining a brain natriuretic peptide/NT-proBNP level at baseline may be useful in monitoring women at risk for decompensated heart failure. Women with systolic dysfunction should be closely monitored for signs of volume overload during the postpartum period, with a low threshold for diuretic administration in women with evidence of intravascular hypervolemia. Standard heart failure management with diuresis, ACE inhibition and beta-blockade is recommended for postpartum women with heart failure. Data are not available regarding safety of ARB or ARNI while breastfeeding. Aldosterone antagonists such as spironolactone are contraindicated during pregnancy due to hormonal effects on the male fetus in animal models but may be used during breastfeeding. Breastfeeding should not be discouraged, nor should necessary medical therapies be withheld due to the desire to breastfeed.

Preconception counseling

Women with a history of cardiomyopathy should undergo a careful review of prior history, diagnostic testing and medication use. Evaluation should include assessment by a cardiologist with expertise in cardiovascular disease in pregnancy as well as a maternal fetal medicine specialist. Additional risk assessment is described in Figure 2.

Contraception

Discussion of contraception is critically important in all women with cardiomyopathy due to particularly high rates of maternal and neonatal morbidity and mortality associated with cardiomyopathies in pregnancy. This is further complicated by increased risk of left ventricular (LV) thrombus formation in the postpartum period in these women. Highly effective methods of contraception are recommended. For complete discussion of contraception, refer to part 5 of this series.

Specific Disorders

Peripartum Cardiomyopathy

Peripartum cardiomyopathy (PPCM) is a specific type of systolic heart failure that occurs towards the end of pregnancy or in the months that follow. The diagnosis is made when the LV ejection fraction (LVEF) is ≤45% in the absence of pre-existing heart disease or other identifiable causes of heart failure. PPCM should be suspected in any woman in late pregnancy or the postpartum period with new onset symptoms of heart failure (22). Management of PPCM overall is similar to the treatment of heart failure with reduced LVEF of other etiologies, with diuresis, afterload reduction, and beta-blockade (22). Though ACE inhibitors, ARBS and ARNIs should be avoided during pregnancy, several ACE inhibitors, including enalapril, captopril, and quinapril, are safe to use while breastfeeding (23). Bromocriptine has been studied to target prolactin blockade as a treatment for peripartum cardiomyopathy, however large-scale evidence-based data to support its use is lacking, with studies are ongoing.

Hypertrophic Cardiomyopathy

Most women with hypertrophic cardiomyopathy have uncomplicated pregnancies, though there is increased risk of symptomatic heart failure and arrhythmias, particularly ventricular arrhythmias, and sudden cardiac death (24-26). Pregnancy is contraindicated in the setting of severe LV dysfunction or severe symptomatic LVOT obstruction (27). Overall management of hypertrophic cardiomyopathy is similar to other etiologies of heart failure but notable differences, including considerations related to the potential for left ventricular outflow tract obstruction, are shown in Table 3.

Hypertensive Disorders of Pregnancy

Prevalence and Epidemiology

Hypertensive disorders of pregnancy (HDP) are the most common adverse pregnancy outcome, affecting 5-10% of women, and are associated with risk for long term CVD (28). A prior history of preeclampsia, renal disease, autoimmune disease, diabetes mellitus, and chronic hypertension are all associated with a heightened risk of preeclampsia and are indications for low dose aspirin prophylaxis as primary or secondary prevention during pregnancy (29). There are marked racial/ethnic disparities in the prevalence of HDP with Black and American Indian/Alaskan Native women bearing the brunt of disease and risk factor burden in the setting of historic and ongoing systemic racism. Interventions to reduce these disparities are urgently needed.

Classification of HDP

HDP include chronic hypertension, gestational hypertension, preeclampsia, and chronic hypertension with superimposed preeclampsia. Currently cardiovascular professional societies recommend a threshold of 130/80 mm Hg for the diagnosis of hypertension, which is lower than the current ACOG guidelines for pregnant women (Figure 3) (29). There are currently evidence gaps as to how best to manage pregnant women with stage 1 hypertension (130-139 /80-89 mm Hg) prior to 20 weeks of gestation, and presently ACOG does not recommend initiation of antihypertensive medication but suggests heightened observation for the development of overt HDP.

Preconception Assessment

Preconception counseling for women with chronic hypertension includes assessment for target-organ involvement and evaluation for secondary causes as clinically indicated. Modifiable CVD risk factors should be optimized before pregnancy and women should be made aware of the state of available evidence regarding various medication classes available. When possible, transitioning to preferred agents is recommended in place of an ACE-I, ARB, or mineralocorticoid receptor antagonist. Lastly, women need to be made aware of the maternal and fetal risks associated with chronic hypertension, including increased maternal risk of gestational diabetes, CVD, and delivery complications as well as fetal complications including preterm birth and restricted fetal growth.

Management

Management of hypertension during pregnancy should mirror treatment in non-pregnant patients in regards to diet and lifestyle modification. Bed rest, restriction of physical activity, weight loss, and extremely low-sodium diets (less than 100 mEq/day) should not be used for the treatment of hypertension or prevention of preeclampsia. Antihypertensives of choice in pregnancy are labetalol, nifedipine and alpha-methyldopa (Table 4). Blood pressure is expected to decline during the first and second trimesters, thus antihypertensive medications may be able to be reduced or stopped in some women with chronic hypertension in this phase. For pregnant women with severe hypertension, defined as systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg, antihypertensive therapy is recommended, however noting that overly aggressive blood pressure lowering is discouraged due to concern for impairing uteroplacental perfusion(30). Target blood pressures range from 120-160/80-110 mmHg with lower treatment thresholds in women with underlying cardiovascular conditions or end organ damage (30).

Management of Acute and Severe Hypertension

Systolic blood pressure ≥ 160 mmHg or diastolic blood pressure ≥ 110 mmHg for > 15 minutes is an obstetric emergency and requires urgent administration of anti-hypertensive medications to reduce the risk of maternal stroke. Intravenous labetalol and hydralazine are first-line options for therapy. Immediate release oral nifedipine may also be considered when IV access is not available (31). Clinicians can refer to the 2019 ACOG hypertension toolboxes for specific sample order sets for management of severe intrapartum or postpartum hypertension (31). Target blood pressure goal is 140-150/90-100 mmHg in a pregnant or postpartum woman with acute severe hypertension which can be modified if there are comorbid cardiovascular conditions.

Postpartum Management and Considerations for Lactation

While blood pressure normally decreases within 48 hours postpartum, blood pressure may increase again between postpartum days 3-6 due to fluid shifts, requiring close monitoring of women at risk for hypertensive complications. Preeclampsia may occur *de novo* postpartum, often presenting with headaches or visual changes in addition to elevated blood pressure(32). These women require prompt treatment, as they are at increased risk of stroke, seizures, pulmonary edema, renal failure, congestive heart failure, and death (32). Post-partum blood pressure evaluation is recommended within 72 hours, and no later than within 10 days after hospital discharge. Preferred agents in regards to lactation are listed in Table 5.

Ischemic Heart Disease

Prevalence and Epidemiology—The prevalence of ischemic heart disease in women who become pregnant is unknown. In the most recent ROPAC study, ischemic heart disease accounted for less than 2% of maternal cardiac conditions (33). However, as maternal age has advanced over time, the likelihood of pre-existing ischemic heart disease at the time of pregnancy is expected to increase as well. Clinicians should remain suspicious of myocardial infarction (MI) in peripartum women with chest pain or acute onset shortness of breath, and in those with cardiac arrest, even in the absence of diagnostic electrocardiographic changes.

Preconception Evaluation

Women with a history of obstructive coronary disease or MI are at elevated risk of cardiac complications during pregnancy although the data are limited. The CARPREG II study noted an approximate 5-7% risk of adverse cardiac events in women with a history of IHD although other studies have estimated up to a 32% risk of cardiovascular complications (34,35). Risk discussion should include details of prior CAD/MI history including prior intervention and review of medications.

Contraception

There are few data to guide considerations for contraception in women with history of IHD. However, considering the significant concerns regarding recurrent risk of coronary dissection with pregnancy, highly effective contraception including the intrauterine device, subdermal implant and permanent sterilization should be considered, and contraceptive formulations containing estrogen should be avoided.

Pathophysiology and Prognosis

When approaching the pregnant patient with acute MI, it is essential to consider non-atherosclerotic conditions, particularly coronary dissection, emboli from hypercoagulable state and other etiologies including coronary spasm, takotsubo syndrome and potential alternative diagnoses of aortic dissection and myocarditis. Inpatient mortality rates for pregnancy-associated MI is 4.5% and similar for STEMI and NSTEMI (36). Mortality is highest among women who sustain an MI during hospitalization for labor and delivery (36-38). The decision process around selection for invasive management is discussed below noting that invasive management has been associated with lower in-hospital mortality (36).

Management

Management of pregnant women with IHD and MI is challenging, necessitating close interaction among cardiologists, obstetricians, and intensivists, Figure 4. Coronary angiography remains the gold standard for diagnosis and treatment of the cause of MI. The risk of fetal compromise decreases in an inversely proportional manner to gestational age (risk being highest prior to 20 weeks) and is proportional to radiation dose (risk is lowest at < 200mGy) with no reports of fetal anomalies or loss when exposure is < 50mGy (39,40). Most coronary angiography and associated percutaneous coronary interventions can be performed well under these dose limits and radiation exposure to the fetus itself is estimated at 20% (41). Thus, if coronary angiography is clinically indicated it should be performed but with every effort to reduce radiation exposure such as reducing fluoroscopic frame rate and avoiding steep angulated views, Figure 4.

Medication

In women with a recent history of percutaneous coronary intervention (PCI), details of the revascularization procedure with regard to lesion location, stent type (drug-eluting or bare-metal) and date of intervention should be documented. Low-dose aspirin is part of standard dual anti-platelet therapy after PCI and is felt to be safe during pregnancy. The risks of premature discontinuation of dual anti-platelet therapy outweigh the risks of fetal harm from

continuation. Recommendations for consideration of medications in IHD are noted in Table 6.

Delivery

As in non-pregnant patients, patients with IHD may be sensitive to excessive derangements in hemodynamics. However, conditions that limit coronary perfusion or increase myocardial oxygen demand during delivery could be particularly harmful in pregnant women who require an increase in blood volume to accommodate the growing fetus (Table 7). Anti-platelet therapy such as clopidogrel, prasugrel and ticagrelor should be held for 5 to 7 days prior to delivery.

Specific Disorders

Acute Coronary Syndrome (ACS)

The treatment of ACS during pregnancy is similar to standard guidelines, with additional considerations for fetal and maternal safety required. Collaboration between obstetric and cardiology services is essential, and management in an intensive care unit should be considered. Urgent delivery of a viable fetus may be required in the event of maternal deterioration.

Medication.—Standard medical therapy for ACS/AMI may need modification in the peripartum period. Morphine does not have teratogenic effects but can cause neonatal respiratory depression if given close to delivery. Heparin does not cross the placenta and is considered safe during pregnancy, but has to be discontinued before delivery. P2Y12 inhibitors have to be held seven days prior to regional anesthesia to reduce the risk of epidural hematoma, though low-dose aspirin does not (42). Nitrates are considered acceptable for use, with close monitoring to avoid hypotension.

Medical Management and PCI.—As with non-pregnant patients, pregnant women presenting with STEMI or unstable NSTEMI should be offered primary PCI (43). Low risk pregnant women with NSTEMI who are hemodynamically stable, without ongoing ischemia, and with normal left ventricular function may be considered for medical management. Women with STEMI and high risk or unstable NSTEMI should undergo invasive strategy regardless of pregnancy status.

Thrombolysis.—Thrombolytic therapy is relatively contraindicated during pregnancy and should only be used in emergency situations when primary PCI is not available as use may worsen coronary artery dissections, which accounts for a significant portion of peripartum ACS.

Spontaneous Coronary Artery Dissection (SCAD)

SCAD commonly results from intramural hemorrhage and more than two-thirds of cases during pregnancy occur postpartum although SCAD may occur at any stage of pregnancy. Women with pregnancy associated SCAD (P-SCAD) often have more severe presentations including hemodynamic instability and multivessel dissections (44). In regard to risk factors,

women with P-SCAD are more likely to have history of fertility therapy, multiparity and preeclampsia.

Preconception counseling in women with history of SCAD

The data on safety of pregnancy in women with prior history of SCAD are limited. The recurrence rate was approximately 15%, in the largest series to date, but this only included 32 pregnancies after a SCAD event (45). Considering the unpredictable nature of SCAD, recommendations regarding risk stratification in pregnancy are unclear. If a woman with a history of SCAD desires pregnancy, LV function, medications and detailed history of SCAD should be reviewed by a multidisciplinary cardio-obstetrics team.

Coronary Angiography and Management of SCAD

Management of P-SCAD is similar to SCAD in non-pregnant patients however outcomes in pregnancy are worse thus necessitating particular care in evaluation and management, Figure 5. Conservative therapy is preferred in most stable P-SCAD patients, as PCI has often been associated with propagation of dissections. Mechanical support with intra-aortic balloon pump can be considered in hemodynamically unstable women. Intravenous heparin is routinely administered in acute coronary syndrome patients but should be discontinued once P-SCAD is identified.

Conclusion

Women with pre-existing acquired cardiovascular disease require thorough evaluation and risk stratification prior to conception. During pregnancy, careful attention should be paid to preservation of maternal stability as this is paramount to optimizing fetal health. Considering the complexity of such cardiovascular conditions, multidisciplinary care is critical involving such subspecialties within cardiology such as heart failure, interventional and electrophysiology.

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Abbreviations

VT	Ventricular Tachycardia
SVT	Supra-Ventricular Tachycardia
PCI	Percutaneous Coronary Intervention
MI	Myocardial Infarction
ACS	Acute Coronary Syndrome
PPCM	Peripartum Cardiomyopathy
LVEF	Left Ventricular Ejection Fraction
SCAD	Spontaneous Coronary Artery Dissection
NYHA	New York Heart Association
MFM	Maternal-Fetal Medicine

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Highlights

- Acquired forms of cardiovascular disease account for considerable morbidity and mortality among pregnant women.
- Interdisciplinary, team-based care is critical to managing complex acquired cardiovascular disease in pregnant women.
- Optimizing maternal outcomes in pregnant women with cardiovascular disease is crucial to promoting fetal health.

Figure 1. Acute Management of Tachyarrhythmias in Pregnancy.

In general, acute management of tachyarrythmias in pregnancy should be managed per standard protocols with particular considerations during pregnancy as discussed here. ACLS - Advanced Cardiovascular Life Support. CV- Cardioversion. VT- Ventricular Tachycardia. SVT- Supra-Ventricular Tachycardia. AF – Atrial Fibrillation

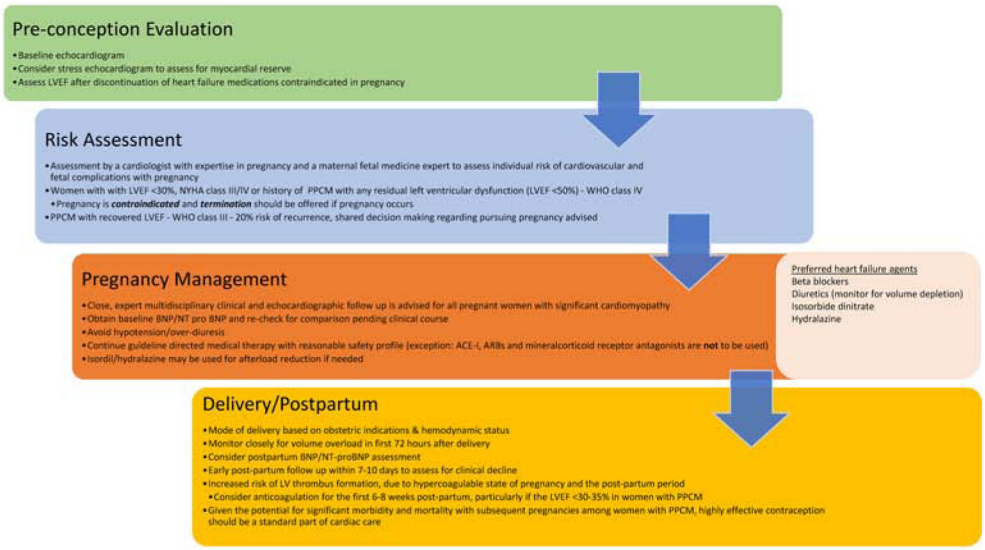


Figure 2. Pre-conception evaluation, counseling and management of cardiomyopathy/heart failure in pregnancy.

Appropriate evaluation and management of pregnant women with known cardiomyopathy is outlined in this figure and is crucial to ensure optimal maternal and fetal outcomes. WHO – World Health Organization. LVEF – Left Ventricular Ejection Fraction. NYHA – New York Heart Association. BNP – Brain Natriuretic Peptide. NT-proBNP – N-terminal-pro hormone BNP. ACE-I – Ace-Inhibitor. ARB – Aldosterone Receptor Blocker. LV – Left Ventricle. PPCM – Peripartum Cardiomyopathy.

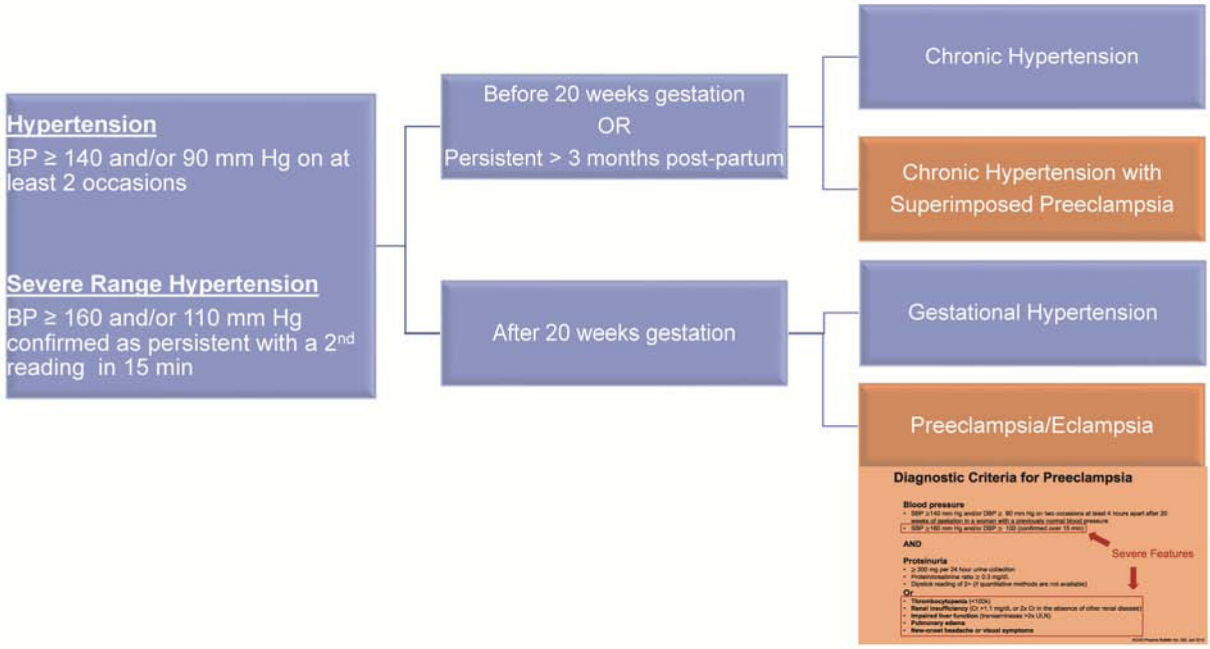


Figure 3. Definitions of Hypertensive Disorders of Pregnancy.

The spectrum of hypertensive disorders of pregnancy are outlined above.

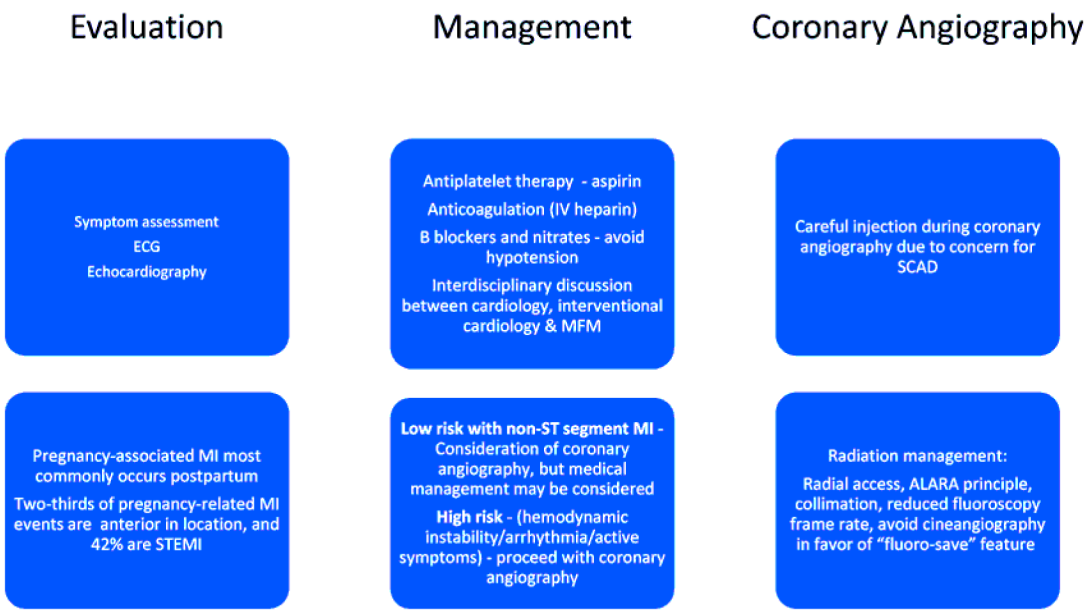


Figure 4. Considerations for evaluation and management of MI during pregnancy.

Management of MI during pregnancy requires interdisciplinary care with considerations for optimizing outcomes while also considering maternal and fetal risk as illustrated here. MI – Myocardial Infarction. ECG – Electrocardiogram. STEMI – ST Elevation Myocardial Infarction. MFM – Maternal-Fetal Medicine. SCAD – Spontaneous Coronary Artery Dissection. ALARA – As Low as Reasonable Achievable.

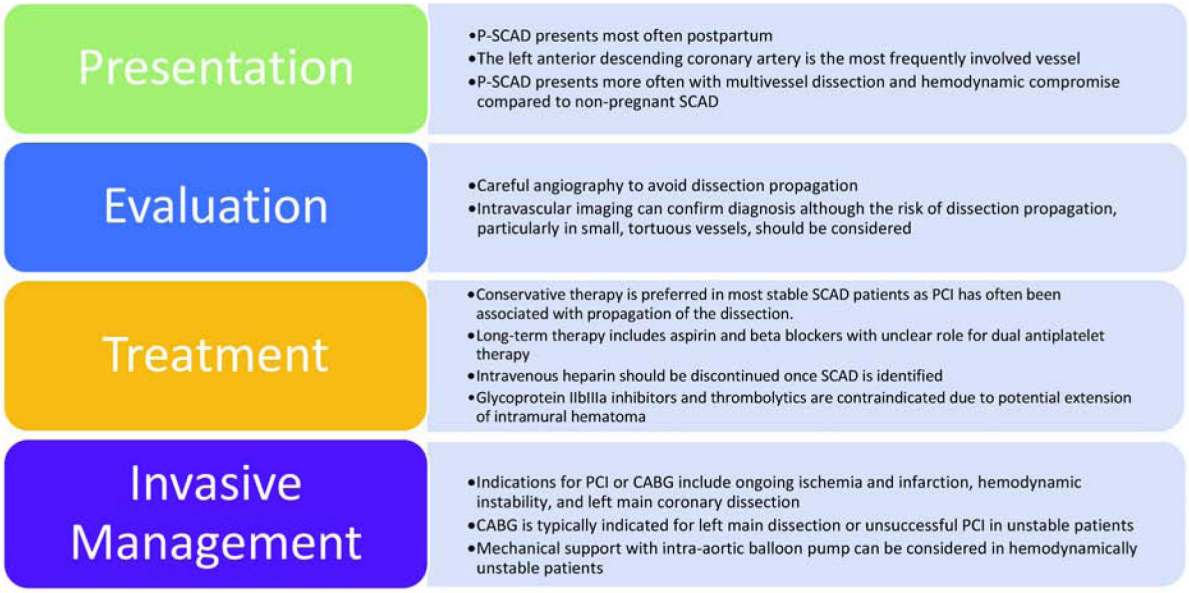
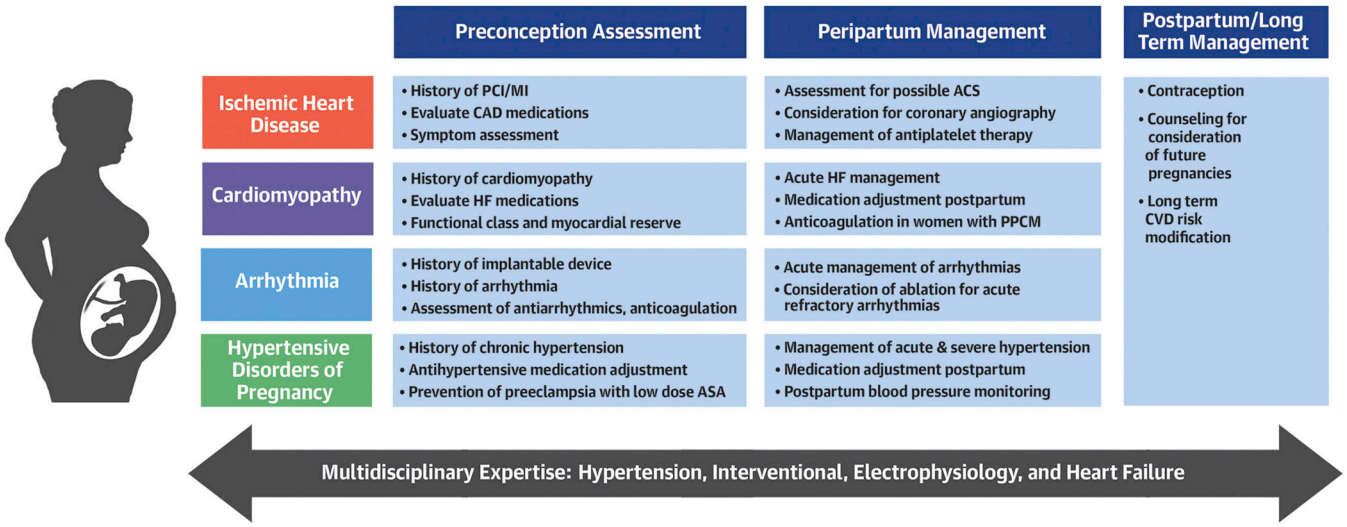


Figure 5. Presentation and Management of SCAD in Pregnancy.

Recognition and management of suspected SCAD in pregnancy requires clinical suspicion and careful assessment during coronary angiography. Considerations for treatment and invasive management are summarized here. SCAD – Spontaneous Coronary Artery Dissection. P-SCAD – Pregnancy-Spontaneous Coronary Artery Dissection. PCI – Percutaneous Coronary Intervention. CABG – Coronary Artery Bypass Grafting.



Central Illustration. Management of Complex Acquired and Heritable Cardiovascular Disease in Pregnancy & Considerations for Subspecialty Cardiovascular Care.

Cardiovascular subspecialties should be included in the assessment and management of various cardiovascular conditions during pregnancy as illustrated in this figure. PCI – Percutaneous Coronary Intervention. MI – Myocardial Infarction. CAD – Coronary Artery Disease. HF – Heart Failure. ASA – Aspirin. ACS – Acute Coronary Syndrome. PPCM – Peripartum Cardiomyopathy. CVD – Cardiovascular Disease.

Table 1.

Contraception in Patients with History of Arrhythmia

- Long Acting Reversible Contraceptives (subdermal implant, levonorgestrel intrauterine device, copper intrauterine device) are safe and effective in the setting of any cardiac arrhythmia.
- Combined hormonal contraceptives (combined oral contraceptive pill, transdermal patch, and vaginal ring) are associated with increased risk of thromboembolism.
  - Caution is advised when using these methods of contraception in women with a history of atrial fibrillation/flutter, even when on anticoagulation.
- Combined hormonal contraceptives may increase warfarin levels; INR monitoring is advised.
- Combined hormonal contraceptives may increase amiodarone levels; QTc monitoring is advised.

Table 2.

Anti-Arrhythmic Medications in Pregnancy and Lactation*

Medication	Previous Categorization	Pregnancy	Lactation
Class Ia			
Quinidine	C		May use while breastfeeding. Excreted in low levels in breast milk; not expected to cause infant harm based on limited excretion into milk.
Procainamide	C		Caution advised while breastfeeding. Excreted in low levels in breast milk; not expected to cause infant harm based on limited excretion into milk.
Disopyramide	C	 Risk of uterine contractions	May use while breastfeeding. Monitor infant for anti-cholinergic effects; may decrease breast milk production.
Class Ib			
Lidocaine	B		May use while breastfeeding. No known risk of infant harm based on limited human data and drug properties. May decrease milk production.
Mexilitine	C		Caution advised while breastfeeding. Excreted in low levels in breast milk; not expected to cause harm in infants older than 2 months; monitor for infant toxicity.
Class Ic			
Flecainide	C		May use while breastfeeding. Excreted in low levels in breast milk; not expected to cause harm in infants based on limited excretion in milk.
Propafenone	C		May use while breastfeeding. Excreted in low levels in breast milk; not expected to cause hard in infant harm based on limited excretion in milk.
Class II			
Metoprolol	C	 bradycardia, hypoglycemia	May use while breastfeeding. No known risk of infant harm based on limited human data and limited excretion in milk.
Atenolol	D	 IUGR, bradycardia, hypoglycemia	Recommend an alternative beta-blocker. Drug excreted extensively in breast milk; risk of bradycardia in the infant; infants older than 3 months appear to be at little risk of adverse effects.
Propranolol	C	 bradycardia, hypoglycemia	May use while breastfeeding. No known risk of infant harm based on human studies. Low levels excreted in breastmilk.
Class III			
Amiodarone	D	 Congenital goiter, bradycardia and QT interval prolongation risk	**May be unsafe.** Excreted in breast milk in variable amounts for weeks, even after mother discontinues medication. Can reduce milk production if mother develops hypothyroidism. Infant may develop hypothyroidism and requires monitoring. No information on iodine levels excreted into breastmilk.

Medication	Previous Categorization	Pregnancy	Lactation
Sotalol	B	bradycardia, hypoglycemia	**May be unsafe.** Extensively excreted in breast milk and renal excretion; infants need to be monitored closely if prescribed. No reports of bradycardia in infants whose mothers were on sotalol.
Ibutilide	C		May use while breastfeeding. No human data available, but infant harm not expected based on drug properties.
Dofetilide	C	Risk of teratogenicity at ≥ 2 mg/kg/d based on animal studies	Possible excretion in breast milk based on drug properties.
Class IV			
Verapamil	C		Caution advised while breastfeeding. Excreted in breast milk in low levels; not expected to harm infants, especially if greater 2 months of age; can cause hyperprolactinemia and galactorrhea.
Diltiazem	C		Caution advised while breastfeeding. <1-2% excreted in breast milk. Not expected to cause infant harm based on drug properties.
Class V			
Adenosine	C		May use while breastfeeding. Has a short half-life; not expected to cause infant harm based on drug properties.
Digoxin	C		May use while breastfeeding. Excreted in breast milk at low levels; no known risk of infant harm based on limited human data. If given intravenously, avoid breastfeeding for 2 hours.

* Sources: LactMed online resource by the National Library of Medicine's TOXNET and epocrates® drug database IUGR: intrauterine growth restriction

= Weigh options, risks vs. benefits

= Use alternative agent

Table 3.

Management of Hypertrophic Cardiomyopathy in Pregnancy

Medications • Beta-blockers should be continued during pregnancy or initiated if new symptoms develop. • Calcium channel blockers including diltiazem and verapamil may be initiated if clinically indicated. • Disopyramide should only be used if the benefits clearly outweigh risks, as it may contribute to uterine contractions.
Evaluation and management • Multidisciplinary clinical and echocardiographic follow up is recommended once per trimester. • Low blood pressure should be promptly evaluated with echocardiography to assess for left ventricular outflow tract obstruction.
Delivery and postpartum • Vaginal delivery with consideration of an assisted second stage is appropriate for most patients, absent an obstetric indication for cesarean delivery. • Single shot spinal anesthesia should be avoided due to the risk of systemic hypotension; slow dosed epidural or combined spinal-epidural anesthesia is preferred. • Patients should be monitored closely post-partum for evidence of volume depletion (e.g., due to blood loss), which can precipitate or worsen left ventricular outflow tract obstruction, and for volume overload. • Continue beta blockade or diltiazem/verapamil through delivery and postpartum.

Table 4.

Preferred Agents for Antihypertensive Treatment in Pregnancy

	Starting Dose	Titration	Maximum Dosage
First Line			
Labetalol	100-200 mg PO BID	Q 2-3 days	2400 mg/24 h
Nifedipine ER	30-60 mg PO Q day	Q 7-14 days	120 mg/24 h
Alpha-methyldopa	250 mg PO BID-TID	Q 2 days	3000 mg/24 h
Second/Third Line			
Hydralazine *	10 mg PO QID	Q 2-5 days	300 mg/24 h
Thiazide diuretics	12.5 mg PO Q day	Q 7-14 days	50 mg/ 24 h
Clonidine	0.1- 0.3mg PO BID 0.1mg transdermal QD	Q 7 days Q 7- 14 days	0.6mg/24 h 0.3mg/24 h
CONTRAINDICATED: ACEI/ARB, Renin Inhibitors, MRAs			
IV therapies for the urgent treatment of severe hypertension in pregnancy			
	Initial Dosage	Dose Titration	
Labetalol	10-20 mg IV	20-80mg IV Q 20-30 min to max 300mg or 1-2 mg/min IV gtt	
Nifedipine IR	10-20 mg PO	Repeat x 1 in 20 minutes, then 10-20mg Q2-6h	
Hydralazine *	5 mg IV or IM	5-10 mg IV Q 20-40min or 0.5-10 mg/h IV gtt	

* do not use in isolation due to potential for reflex tachycardia

ACEI – Ace-Inhibitor, ARB – Angiotensin Receptor Blocker, MRAs – mineralocorticoid receptor antagonists

Table 5.

Antihypertensives & Breast Feeding

Medication Class	**Preferred Agents**
Calcium Channel Blockers	Nifedipine, Verapamil, Diltiazem
Beta Blockers	Labetalol, Metoprolol, and Propranolol are preferred
ACE-I	Captopril, Enalapril, Benazepril, Quinapril
Diuretics	Hydrochlorothiazide, Spironolactone Safe, can decrease milk production *Exception - chlorthalidone due to risk of fetal jaundice, thrombocytopenia, hypoglycemia and electrolyte abnormalities
Methyldopa	Caution! May exacerbate postpartum depression
ARBs	Insufficient data to recommend their use during breast feeding
Clonidine transdermal patch	Caution! Possible infant/lactation effects

Table 6.

Ischemic Heart Disease Medications During Pregnancy and Lactation

Drug	Use in Pregnancy	Lactation	Adverse Effects
Aspirin	First choice anti-platelet agent; also indicated for prevention of premature birth and pre-eclampsia.	Low dose aspirin may be used for cardiovascular indications. Appears in subclinical amounts in human milk.	Safe when dose is below 100 mg. Full dose aspirin: in first trimester may cause 2-3-fold increase risk of gastroschisis; with high dose also risk for premature closure of ductus arteriosus, fetal bleeding risk.
Clopidogrel	May be used for shortest duration necessary. Animal studies do not note adverse effects; limited human data. Must be stopped 7 days prior to regional anesthesia.	Assess risk/benefit. Low risk of infant harm based on limited human data and drug properties.	Not expected to cause congenital anomalies based on animal studies.
Prasugrel Ticagrelor/ Cangrelor	Minimal data; Ticagrelor does cross placenta. Assess risk/benefit. Must be stopped 5-7 days prior to regional anesthesia.	Assess risk/benefit. No human data available, though drug excretion into milk possible based on drug properties.	No reported complications with prasugrel.
Ranolazine	Unknown	Unknown	Maternal toxicity and misshapen sternebrae and reduced ossification in animal studies; no adequate well-controlled studies in pregnant women; current recommendation is used during pregnancy only when potential benefit to patient justify potential risk to fetus
Tirofiban/ eptifibatide	Unknown	Unknown	No current guidelines; not well studied; there is case report stating that it could be safe but not many studies. Eptifibatide's short half-life may allow safe use proximal to delivery.
Beta Blockers Labetalol Atenolol Metoprolol Caivedilol	Metoprolol succinate preferred (avoids interfering with B2-mediated uterine relaxation and peripheral vasodilation). **Atenolol contraindicated**	Assess risk/benefit. Labetalol and metoprolol are safe; carvedilol is unknown risk. Avoid atenolol if possible. Transfer to breast milk in low levels.	Atenolol associated with birth defects/ IUGR
Calcium Channel Blockers Nifedipine Verapamil Diltiazem Amlodipine	Nifedipine is first line for hypertension and tocolysis (when used with magnesium) Verapamil considered fairly safe (second line after beta blockers for rate control and treatment of idiopathic sustained ventricular tachycardia). Amlodipine is probably safe for hypertension	Nifedipine is safe Assess risk/benefit of verapamil and diltiazem. Excreted in milk in low levels, not expected to cause infant harm based on drug properties.	Possible prematurity, IUGR, fetal bradycardia in some CCB Risk of teratogenicity not expected based on limited human data. Has tocolytic effect (delay contraction and suppress labor); can cause maternal hypotension and placental hypoperfusion.
Nitrates	Safe in pregnancy	Weight risks/benefits. Limited data.	Crosses placenta; potential hypotension
Statins	Contraindicated	Contraindicated	Potential teratogenicity; limited human data. Use in first trimester correlated with premature birth.
Bile Acid Sequestrants (cholestyramine and colestipol)	Considered safer than other lipid-lowering agents; treatment of choice for hyperlipidemia	Considered safe. Limited data.	May lower fat-soluble vitamins
ACE inhibitors Angiotensin Receptor Blockers	Contraindicated	Captopril, benazepril and enalapril, quinapril are considered safe. Because of low levels excreted into breastmilk, infant harm is not expected. Conflicting data for ARBS; currently contraindicated	Fetal renal and cardiac abnormalities

Table 7.

Delivery management in pregnant women with IHD

Such conditions as iron deficiency anemia and volume depletion may exacerbate underlying ischemia.
Hypotension should be avoided to limit demand ischemia as well as placental hypoperfusion.
Hypertensive episodes, particularly in the setting of gestational hypertension or pre-eclampsia, should be aggressively treated in pregnant women with IHD to avoid exacerbation of ischemia and increase in afterload.
In regard to mode of delivery, in general, there are no data to suggest that cesarean section is associated with improved outcomes over vaginal delivery in women with IHD.
Overall, vaginal delivery is encouraged whenever possible to avoid infectious risk and excess bleeding with consideration for assisted second stage and efforts to minimize blood loss and reduce tachycardia.
IHD – Ischemic Heart Disease