JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 77, NO. 14, 2021

PUBLISHED BY ELSEVIER

JACC FOCUS SEMINAR: CARDIO-OBSTETRICS

JACC FOCUS SEMINAR

Management of Women With Congenital or Inherited Cardiovascular Disease From Pre-Conception Through Pregnancy and Postpartum

JACC Focus Seminar 2/5

Kathryn J. Lindley, MD,[a] C. Noel Bairey Merz, MD,[b] Anita W. Asgar, MD, MSc,[c] Natalie A. Bello, MD, MPH,[d] Sonal Chandra, MD,[e] Melinda B. Davis, MD,[f] Mardi Gomberg-Maitland, MD, MSc,[g] Martha Gulati, MD, MS,[h] Lisa M. Hollier, MD,[i] Eric V. Krieger, MD,[j] Ki Park, MD,[k] Candice Silversides, MD,[l] Natasha K. Wolfe, MD,[a] Carl J. Pepine, MD,[k] on behalf of the American College of Cardiology Cardiovascular Disease in Women Committee and the Cardio-Obstetrics Work Group

ABSTRACT

Maternal morbidity and mortality continue to rise in the United States, with cardiovascular disease as the leading cause of maternal deaths. Congenital heart disease is now the most common cardiovascular condition encountered during pregnancy, and its prevalence will continue to grow. In tandem with these trends, maternal cardiovascular health is becoming increasingly complex. The identification of women at highest risk for cardiovascular complications is essential, and a team-based approach is recommended to optimize maternal and fetal outcomes. This document, the second of a 5-part series, will provide practical guidance from pre-conception through postpartum for cardiovascular conditions that are predominantly congenital or heritable in nature, including aortopathies, congenital heart disease, pulmonary hypertension, and valvular heart disease. (J Am Coll Cardiol 2021;77:1778–98) © 2021 by the American College of Cardiology Foundation.

Cardiovascular disease is the leading cause of pregnancy-related deaths in the United States (1). Contributing factors include increases in the number of first births to older women and increased prevalence of underlying cardiovascular risk factors in pregnant women (1). Medical and surgical management of pediatric heart disease now permits survival of most women born with congenital

From the [a]Cardiovascular Division, Department of Medicine, Washington University School of Medicine, St. Louis, Missouri, USA; [b]Barbra Streisand Women's Heart Center, Cedars-Sinai Smidt Heart Institute, Los Angeles, California, USA; [c]Division of Cardiology, Institut de Cardiologie de Montreal, Universite de Montreal, Montreal, Quebec, Canada; [d]Department of Medicine, Division of Cardiology, Columbia University Irving Medical Center, New York, New York, USA; [e]Division of Cardiology, Rush University Medical Center, Chicago, Illinois, USA; [f]Division of Cardiovascular Medicine, Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan, USA; [g]George Washington University School of Medicine and Health Sciences, Washington, DC, USA; [h]Department of Medicine (Cardiology), University of Arizona-Phoenix, Phoenix, Arizona, USA; [i]Department of Obstetrics and Gynecology, Baylor College of Medicine, Houston, Texas, USA; [j]Seattle Adult Congenital Heart Service, University of Washington School of Medicine, Seattle, Washington, USA; [k]Cardiovascular Medicine, University of Florida College of Medicine, Gainesville, Florida, USA; and the [l]Division of Cardiology, University of Toronto Pregnancy and Heart Disease Program, Mount Sinai Hospital and University Health Network, University of Toronto, Toronto, Ontario, Canada.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received November 25, 2020; revised manuscript received January 19, 2021, accepted February 12, 2021.

Listen to this manuscript's audio summary by Editor-in-Chief Dr. Valentin Fuster on JACC.org.

ISSN 0735-1097/$36.00 https://doi.org/10.1016/j.jacc.2021.02.026

HIGHLIGHTS

- CHD is the most common cardiovascular condition encountered in pregnant women.
- Most women with congenital and heritable conditions can be safely managed with a team-based approach throughout pregnancy.
- High-risk conditions include pulmonary hypertension, cardiomyopathy, left-sided obstructive valvular disease, and certain aortopathies.
- Long-acting reversible contraception is safe and effective for patients with congenital and heritable cardiovascular conditions.

heart disease (CHD) to reproductive age and beyond (2). This document serves as a practical guide from pre-conception through postpartum for the management of pregnant women with cardiovascular conditions predominantly congenital or heritable in nature, namely aortopathies, CHD, pulmonary hypertension, and valvular heart disease.

CARDIO-OBSTETRICS TEAM AND RISK STRATIFICATION

Pregnancy may be poorly tolerated by women with congenital or heritable cardiovascular conditions. Due to the wide heterogeneity in cardiovascular risk associated with pregnancy, pre-conception risk stratification, and counseling according to the risk models discussed in Part 1 of this series should begin in adolescence and continue into adulthood (3). A multidisciplinary cardio-obstetrics team should ideally evaluate the patient before conception, optimize her cardiac status prior to pregnancy when needed, and follow her through the pregnancy and postpartum period. Members of the cardio-obstetrics team will vary based on the complexity of the patient's underlying cardiac condition, but women with modified World Health Organization class III and IV conditions require a cardio-obstetrics team experienced in the management of complex cardiac disease in pregnancy (see Part 1) (3,4).

AORTOPATHY

Pregnancy can result in weakening of the aortic media, increased aortic diameter and heightened risk of aortic dissection in pregnancy and the postpartum period (5). Aortic complications occur most commonly in the third trimester or postpartum, and risk is further increased in the presence of concomitant hypertension (6). Aortic dissection is associated with high maternal and fetal mortality (8.6% and 50%, respectively), and requires prompt diagnosis and treatment (7).

ABBREVIATIONS AND ACRONYMS

CHD = congenital heart disease
CT = computed tomography
MS = mitral stenosis
PAH = pulmonary arterial hypertension

PRE-CONCEPTION EVALUATION. Patients at risk for aortic aneurysms (**Table 1**) should be evaluated with echocardiogram and computed tomography (CT)/magnetic resonance imaging within 1 year prior to conception to evaluate for aortic valve disease and aortic dimensions. In those with aortic root dilatation exceeding certain diametric thresholds (**Table 1**), consider prophylactic surgery prior to pregnancy. The majority of pregnancy-related aortic complications occur in patients with a family but not a personal history of aortopathy (8). Thus, risk screening and genetic counseling is recommended as a part of the pre-conception evaluation for women with a first- or second-degree relative with aortopathy, given the heritability of these disorders.

PREGNANCY MANAGEMENT. Women with aortopathy syndromes require a multidisciplinary team with expertise in the management of aortic disease during pregnancy. Current guidelines recommend serial aortic imaging throughout pregnancy until 6 months postpartum by echo or noncontrast magnetic resonance angiography (MRA) (9). Blood pressure management during pregnancy to prevent stage II hypertension (140/90 mm Hg) is recommended; consideration should be given to beta-blockade during pregnancy (9). Rapid aortic root expansion during pregnancy (>5 mm) should prompt discussion of therapeutic options, including pregnancy termination versus aortic repair with the fetus in utero prior to viability. When the fetus is viable, Caesarean delivery in a tertiary cardiothoracic center, followed directly by aortic surgery, is recommended. The safest period to undertake semielective surgery is during the second trimester (5). Disease-specific management of heritable aortopathies is summarized in **Table 2** (10–18).

A documented delivery plan should be widely distributed to all health care team members with consideration for delivery at term given the maternal risks of pregnancy continuation versus small additional fetal benefit. Most women may be delivered vaginally with consideration for an assisted second stage in the event of prolonged pushing, although Cesarean delivery may be safer for high-risk women (**Table 2**). Delivery is recommended at a hospital where cardiothoracic surgery is available (9).

TABLE 1 Pregnancy Management for Women With Aortopathy

Condition	mWHO Class	Pre-Conception Surgery	Cesarean Delivery	Imaging Frequency	Heritability	Disease-Specific Features
Bicuspid AV	II: AVA >1 cm^2 and peak gradient <50 mm Hg, aortic root <45 mm	>50 mm	>50 mm	At least once if normal aortic dimension	9%	Aortic dilatation may worsen aortic regurgitation
	III: aortic root 45–50 mm			Every trimester if >40 mm		Fetal echocardiogram recommended second trimester
	IV: AVA <1 cm^2 or peak gradient >50 mm Hg or aortic root >50 mm					
Turner syndrome	II–III: aortic root <20 mm/m^2 with associated risk factors or <25 mm/m^2 without associated risk factors	>25 mm/m^2 or >20 mm/m^2 with associated risk factors for aortic dissection	>20 mm/m^2	At least once if normal aortic dimension	5% CHD	Risk for pregnancy loss, pre-eclampsia, and ~2% risk of dissection
	IV: aortic root >20 mm/m^2 with associated risk factors or >25 mm/m^2 without associated risk factors			Every 4 to 8 weeks if dilated aorta		Pregnancy risk higher for women with structural heart disease and hypertension
Marfan syndrome	III: aortic root <45 mm, mod-severe AI	>40–45 mm	>40 mm	Every 4 to 8 weeks if >40 mm	50%	Dissection risk ~10% if aortic root >40 mm, ≤1% if aortic root <40 mm; more recent studies suggest up to 4.5 cm may be safe
	IV: aortic root >45 mm, history of dissection	Moderate-severe aortic regurgitation	History of aortic dissection	Every trimester if <40 mm		Pregnancy discouraged if high risk features: personal or family history of dissection, rapid dilation rate
		Rapid dilatation (>2 to 3 mm/yr)				
Vascular Ehlers-Danlos	IV	No well-established guidelines, >40 mm reasonable	All—to reduce risk of obstetric complications	Every 4 to 8 weeks	50%	Mortality 5.3%, life-threatening complications in 14.5%—pregnancy should be avoided Significant obstetric morbidity—uterine rupture, premature rupture of membranes with pre-term delivery, antepartum and postpartum hemorrhage, and severe perineal tears Delivery recommended by 36 to 38 weeks
Loeys-Dietz	III: aortic diameter <40 mm	>42 mm by TEE or >44 to 46 mm by CT or MRA	>40 mm	Every 4 to 8 weeks	50%	Pre-conception comprehensive MRA/CTA of brain, pelvis, thorax, and abdomen recommended
	IV: aortic diameter >40 mm	*No diameter is truly safe				More aggressive vascular course than Marfan syndrome—dissection may occur in absence of aneurysm
Familial thoracic aortic aneurysms and dissections	III: aortic diameter <40 mm			Every trimester if <40 mm	Variable	Dissection may occur with minimal aortic dilatation
	IV: aortic diameter >40 mm			Every 4–8 weeks if >40 mm		Dissection may occur in descending aorta after replacement of ascending aorta

Although each patient requires individualized management, this table provides general disease-specific recommendation for the management of women with heritable aortopathy.

AI = aortic insufficiency; AV = aortic valve; AVA = aortic valve area; CHD = congenital heart disease; CTA = computed tomography angiography; MRA = magnetic resonance angiography; mWHO = modified World Health Organization.

EMERGENCY MANAGEMENT. Noncontrast MRA or contrast-enhanced computed tomography angiography (CTA) should be performed immediately upon suspicion of aortic dissection. Emergency surgery should be undertaken regardless of trimester for acute type A aortic dissections. In women with a viable fetus, Caesarean delivery should be performed immediately before the aortic repair, given the fetal risks associated with cardiopulmonary bypass. Type B aortic dissections are usually managed medically unless there are end-organ complications, in which case endovascular strategies should be considered. Gravid or postpartum patients should be managed in a tertiary care center specializing in management of aortic complications.

TABLE 2 Pregnancy Management for Women With Congenital Heart Disease

CHD Lesion	WHO Class	Potential Complications	Monitoring Considerations	Management Considerations	Anesthesia Considerations	Delivery Considerations	Postpartum Considerations
Shunt Lesions (ASD, VSD, PDA)							
Repaired	I	Arrhythmias	Baseline echo	After initial cardiology consultation, may be managed at nonspecialized center	Consider epidural	Vaginal preferred	Low risk for complications
Unrepaired Qp:Qs <1.5	II	Arrhythmias, heart failure, paradoxical embolism	Baseline and 28- to 32-week echocardiogram	Consideration of aspirin 81 mg or prophylactic enoxaparin for paradoxical embolism prevention	Potential to transiently reverse shunt with systemic hypotension Filtered IV lines Consider epidural	Vaginal preferred	Small risk of right heart failure; risk of paradoxical embolism
Unrepaired Qp:Qs >1.5	II	Arrhythmias, heart failure, paradoxical embolism	Consider serial echo to monitor ventricular function and pulmonary pressures	Consideration of aspirin 81 mg or prophylactic enoxaparin for paradoxical embolism prevention	Preload dependent if RV enlargement/ dysfunction Potential to transiently reverse shunt with systemic hypotension Filtered IV lines Epidural recommended	Vaginal preferred unless severe pulmonary hypertension	Risk of right heart failure and paradoxical embolism
Systemic right ventricle							
D-TGA with atrial switch, L-TGA	III	Atrial arrhythmias (15%), heart failure (10%), worsening tricuspid regurgitation, premature delivery (33%), accelerated decline in systemic ventricular function	Baseline and 28- to 32-week echocardiogram	Requires CHD cardiologist and MFM	Epidural recommended—slow titration if significant systemic ventricular dysfunction	Vaginal preferred unless acute decompensated heart failure	Risk of postpartum heart failure—consider extended postpartum monitoring 48 to 72 h
			Holter/event monitoring for palpitations	Continue heart failure therapies with pregnancy-safe medications Continue arrhythmia management with pregnancy-safe medications	Consider telemetry monitoring	Delivery in specialized CHD/ cardio-obstetrics care center	Early postpartum outpatient follow-up
D-TGA with arterial switch	II-III	Arrhythmias (2.5% to 7%), heart failure (2.5% to 21%)	Baseline echo Consider baseline ischemic evaluation if any chest pain symptoms Consider 28- to 32-week echo if significant PI, AI or ventricular dysfunction	Recommend CHD cardiologist, MFM management	Consider epidural Consider telemetry monitoring	Vaginal preferred	Low risk of postpartum arrhythmias or heart failure
Tetralogy of Fallot	II	Arrhythmias (2% to 6%), heart failure (2%), progressive right heart failure/ dysfunction	Baseline echo to evaluate pulmonary valve and right ventricular function	Recommend CHD cardiologist and MFM management	Epidural recommended—slow titration if significant right ventricular dysfunction	Vaginal preferred	Risk of right heart failure if significant pulmonary valve or right heart dysfunction

Continued on the next page

TABLE 2 Continued

CHD Lesion	WHO Class	Potential Complications	Monitoring Considerations	Management Considerations	Anesthesia Considerations	Delivery Considerations	Postpartum Considerations
		*Risk higher for women requiring cardiac medications prior to pregnancy, ≥moderate pulmonary regurgitation, or severe RV dilation	Consider 28- to 32-week echocardiogram if significant pulmonary valve or right ventricular dysfunction	Consider genetics consultation given increased risk of fetal transmission of conotruncal defects	Consider telemetry monitoring		
				If asymptomatic and good functional capacity, pre-conception PVR not required unless otherwise meeting indication			
Coarctation of the aorta	II–III	Hypertensive disorders of pregnancy (30%), aortic dissection if aneurysm present	Baseline MRA	Consider aspirin 81 mg daily beginning in the second trimester given increased risk of pre-eclampsia	Epidural recommended	Vaginal generally preferred	High risk of postpartum hypertension—blood pressure expected to peak between days 3 to 8 after delivery
		*Increased risk for complications if any of the following: residual obstruction (gradient >20 mm Hg, minimal aortic lumen <12 mm), hypertension, aortic aneurysm	Consider serial noncontrast MRA if aortic diameter >4.0 cm	Close monitoring of blood pressure with individualized blood pressure goals, considering risk of cerebral hypertension and fetal hypoperfusion in the setting of underlying residual coarctation		Consider Cesarean delivery if ascending aortic aneurysm >5.0 cm or acute aortic syndrome	
			Baseline echo to evaluate for bicuspid aortic valve	Repair residual/recurrent coarctation prior to pregnancy if possible			
			Baseline MRA brain to evaluate for berry aneurysms	Consider repair of aortic aneurysm >5.0 cm prior to pregnancy			
Severe unrepaired coarctation	IV			Coarctation should be repaired prior to proceeding with pregnancy			
Single-ventricle physiology	III	Atrial arrhythmias, heart failure, thromboembolism, fetal loss, growth restriction, preterm birth	Baseline echocardiogram, pre-conception exercise test.	Requires coordinated care by CHD cardiologist and MFM	Epidural is recommended—slow titration due to pre-load–dependent circulation	Vaginal preferred	Remains at risk of heart failure and thromboembolism
	IV: evidence of Fontan failure, clinically significant cirrhosis, baseline hypoxemia, poor functional class	Live birth rate only 45% if evidence of Fontan failure	Consider 28- to 32-week echocardiogram	Continue heart failure therapies with pregnancy-safe medications	IV filters required if Fontan fenestration or significant venovenous collaterals	Labor in left lateral decubitus position due to pre-load dependence	
			Baseline labs—liver function tests, renal function tests, liver imaging, pulse oximetry	Continue arrhythmia management with pregnancy-safe medications		Consider low threshold for assisted second stage to reduce duration of Valsalva	

Continued on the next page

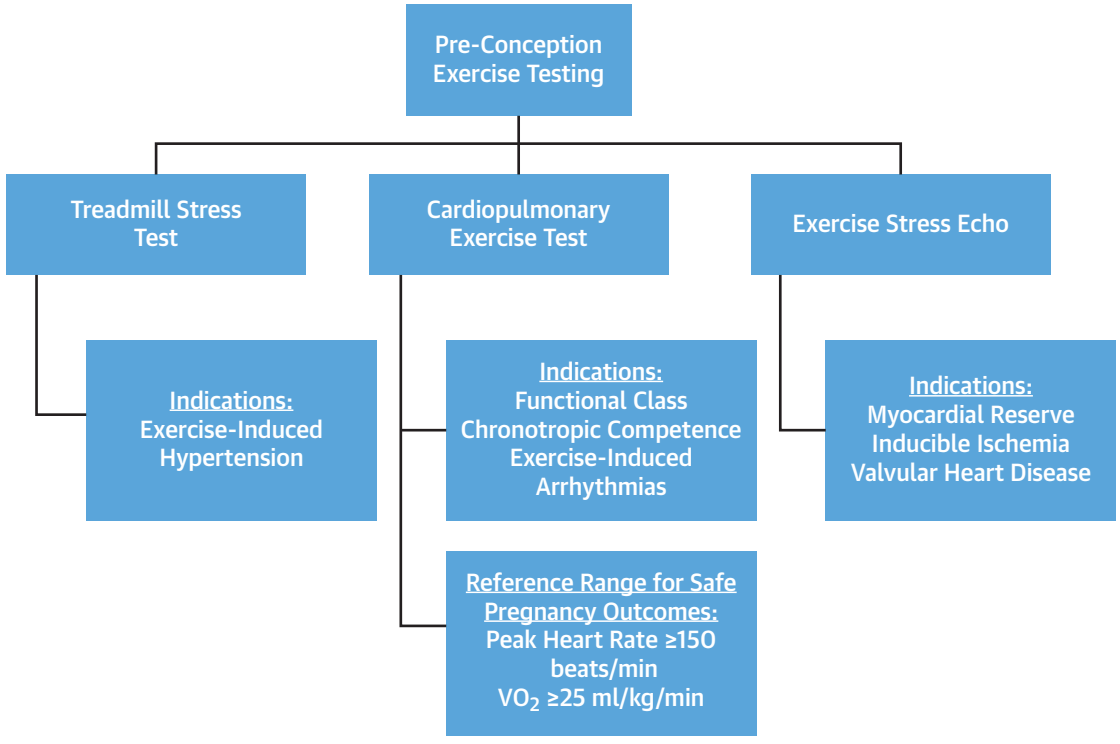
TABLE 2 Continued

CHD Lesion	WHO Class	Potential Complications	Monitoring Considerations	Management Considerations	Anesthesia Considerations	Delivery Considerations	Postpartum Considerations
			Consider pre-conception cardiopulmonary stress test to assess functional capacity	Consider low-dose aspirin, prophylactic, or therapeutic anticoagulation to prevent thromboembolism, depending on type of palliation, degree of cyanosis, and history of thromboembolism		Maintain adequate hydration and treat hypotension or hemorrhage with immediate fluid resuscitation	
			Consider baseline endoscopy if evidence of portal hypertension; consider repeating second trimester if evidence of varices				

Although each patient requires individualized management, this table provides general disease-specific recommendation for the management of women with congenital heart disease.

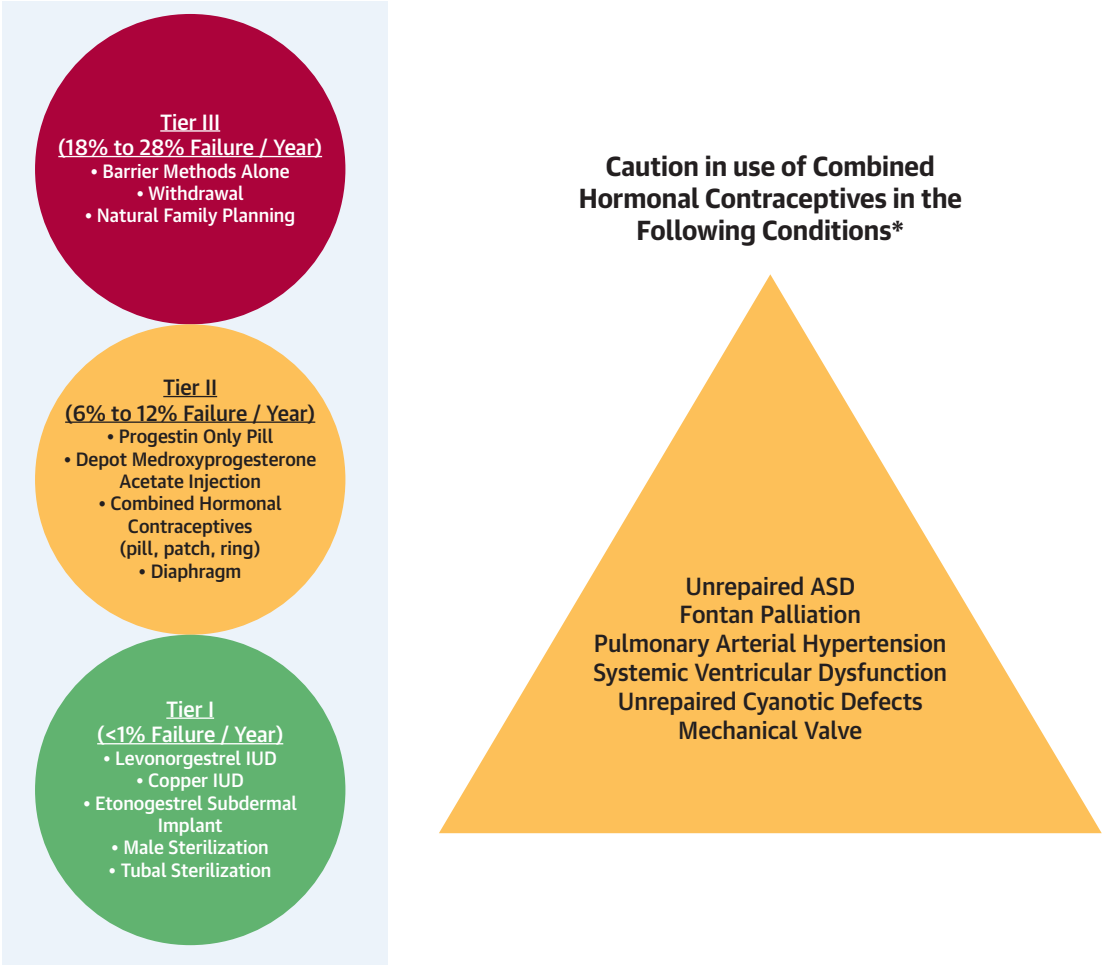
ASD = atrial septal defect; CHD = congenital heart disease; IV = intravenous; MFM = maternal fetal medicine; MRA = magnetic resonance angiography; PDA = patent ductus arteriosus; PI = pulmonary insufficiency; PVR = pulmonary valve replacement; RV = right ventricle; TGA = transposition of the great arteries; VSD = ventricular septal defect; WHO = World Health Organization.

FIGURE 1 Algorithm for Pre-Conception Stress Testing for Women With CHD



Pre-conception exercise testing may be considered for risk stratification, in particular for women with congenital or valvular conditions. VO_2 = maximum oxygen consumption.

FIGURE 2 Safety and Efficacy of Contraceptives in Women With CHD



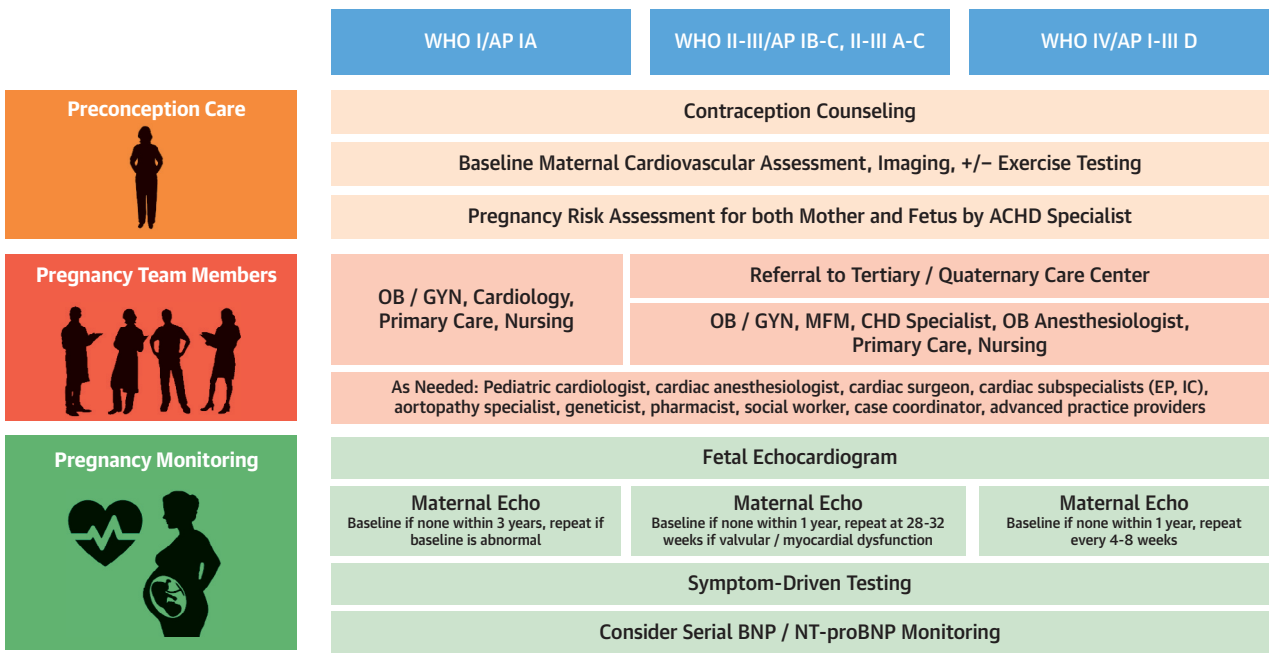
Long-acting reversible contraceptives (the IUD and subdermal implant) and permanent sterilization are safe and highly effective for all women with CHD. Caution should be advised when prescribing combined hormonal contraceptives to women with certain CHD conditions due to the increased risk of thromboembolism. *Remember that combined hormonal contraceptives are still lower risk than pregnancy, so always weigh risk/benefit ratio and establish another highly effective method of contraception before stopping. ASD = atrial septal defect; CHD = congenital heart disease; IUD = intrauterine device.

CONGENITAL HEART DISEASE

The risk of severe maternal morbidity or mortality depends on the type of CHD, severity of residual lesions, and ventricular function (19). Mortality in the Registry of Pregnancy and Cardiac Disease CHD population was 0.2%, with heart failure occurring in 13% of patients with complex CHD and in 5% with simple to moderate CHD (19). Women with complex CHD are also at increased risk of obstetric and fetal complications, including postpartum hemorrhage, spontaneous pre-term birth, and small for gestation age babies (20,21). Individual pre-conception risk stratification is thus essential for counseling and managing patients during their childbearing years (2).

PRE-CONCEPTION EVALUATION. Discussions regarding contraception and pregnancy should begin in pediatric cardiology clinics and continue after transition to adult CHD care (3,22). Residual or progressive lesions are common, and pre-conception imaging is important for identifying high-risk lesions, such as pulmonary hypertension, severe left-sided obstructive valve disease, systemic ventricular dysfunction, or aortic dilation (23). When possible, high-risk lesions should be treated prior to conception (23).

CENTRAL ILLUSTRATION **Multidisciplinary Cardio-Obstetrics Team Management for Women with Congenital Heart Disease**



Lindley, K.J. et al. J Am Coll Cardiol. 2021;77(14):1778–98.

The ACHD Anatomy + Physiological Stage Classification scheme is based on simple, moderate, or great anatomical complexity (I, II or III respectively) and increasingly severe stages of abnormal physiology (A to D). The AP Stage Classification is outlined in detail in the 2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease (3). ACC = American College of Cardiology; AHA = American Heart Association; AP = ACHD Anatomy + Physiological Stage Classification; BNP = brain natriuretic peptide; CHD = adult congenital heart disease; EP = electrophysiology; IC = interventional cardiology; MFM = maternal-fetal medicine; NT-proBNP = N-terminal-pro hormone brain natriuretic peptide; OB/GYN = obstetrics and gynecology; WHO = World Health Organization.

Pre-conception exercise testing can help with risk stratification, particularly in patients with current or recovered ventricular dysfunction or valve disease (**Figure 1**) (3,23,24). Referral to a geneticist for risk assessment is appropriate for women with high risk for fetal transmission of cardiovascular disease or a strong family history of CHD.

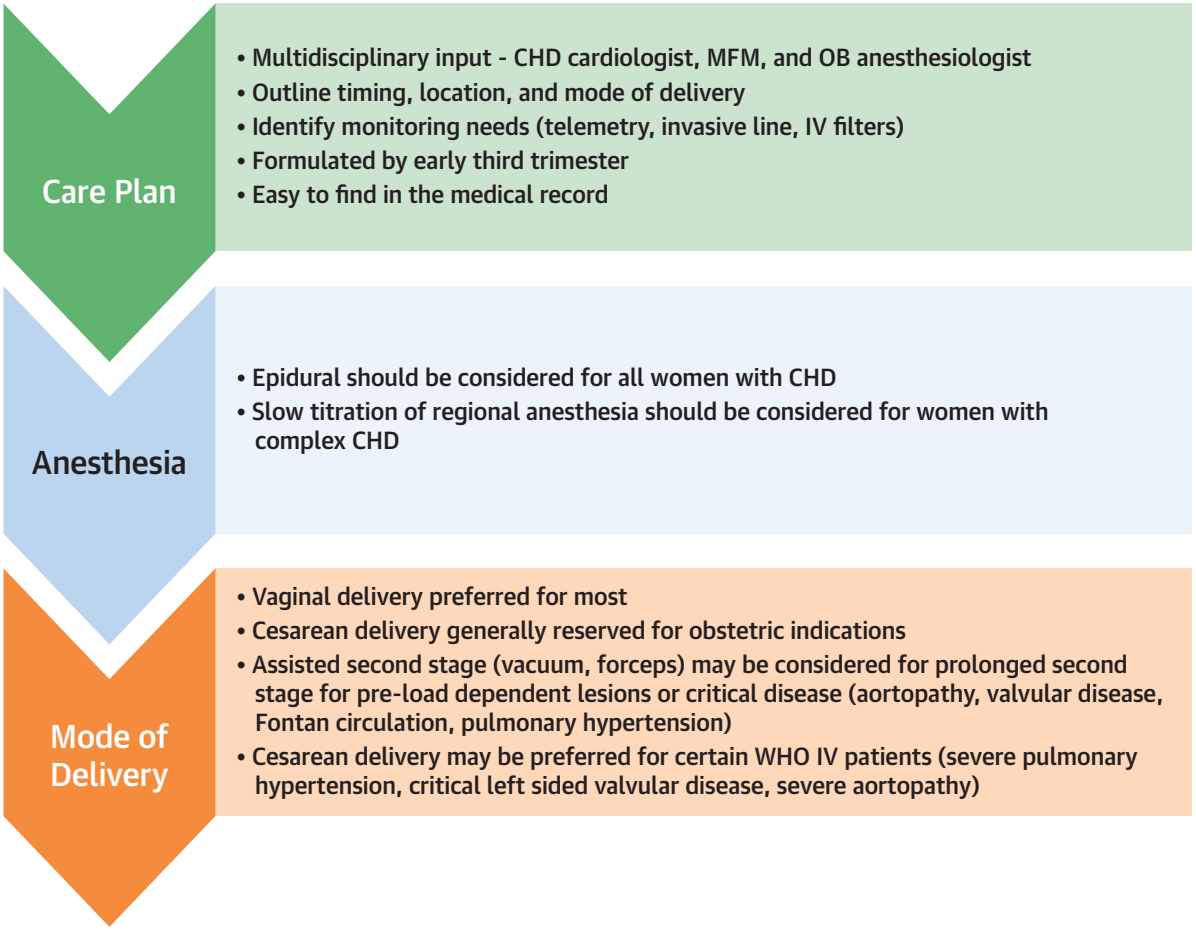
CONTRACEPTION. Contraception is discussed in detail in Part 5 of this series. Long-acting reversible methods of contraception are safe for women with all forms of CHD (25). Combined hormonal contraceptives are considered contraindicated in patients with CHD who are at high risk for thromboembolism and in those with prosthetic valves, and alternate methods of contraception should be considered (**Figure 2**) (26).

FETAL SCREENING. The risk of CHD in a child born to a parent with nonsyndromic CHD is approximately 3% to 5%, compared with 1% in the general population (27). Certain cardiac defects are associated with higher rates of fetal transmission. A dedicated fetal echocardiogram should be performed between gestational weeks 18 and 22 when either parent has a history of CHD (3,27).

PREGNANCY MANAGEMENT. Each patient requires an individualized pregnancy management plan developed by a cardio-obstetrics team that includes specialists from adult congenital cardiology, maternal fetal medicine, obstetric anesthesiology, and pediatric cardiology if the fetus also has CHD (**Central Illustration**) (3). Although each patient will require individualized care plans based on her specific anatomy and physiology, general disease-specific management is outlined in **Table 2** (23,26,28–36).

DELIVERY PLANNING. Due to the increased risk of spontaneous pre-term birth, the multidisciplinary team should document a detailed delivery care plan by 28 weeks, which is easy to find in the medical record (**Figure 3**) (3). Vaginal delivery is preferred for the majority of patients, with consideration of an assisted second stage for those with critical disease, aortopathy, or pre-load-dependent conditions such as pulmonary hypertension or Fontan circulation

FIGURE 3 Delivery Planning in Women With CHD



The multidisciplinary cardio-obstetrics team should collaborate to develop a delivery plan by the early third trimester. The delivery plan should include recommendations for anesthesia, monitoring, and timing/mode of delivery. CHD = congenital heart disease; IV = intravenous; MFM = maternal fetal medicine; OB = obstetric; WHO = World Health Organization.

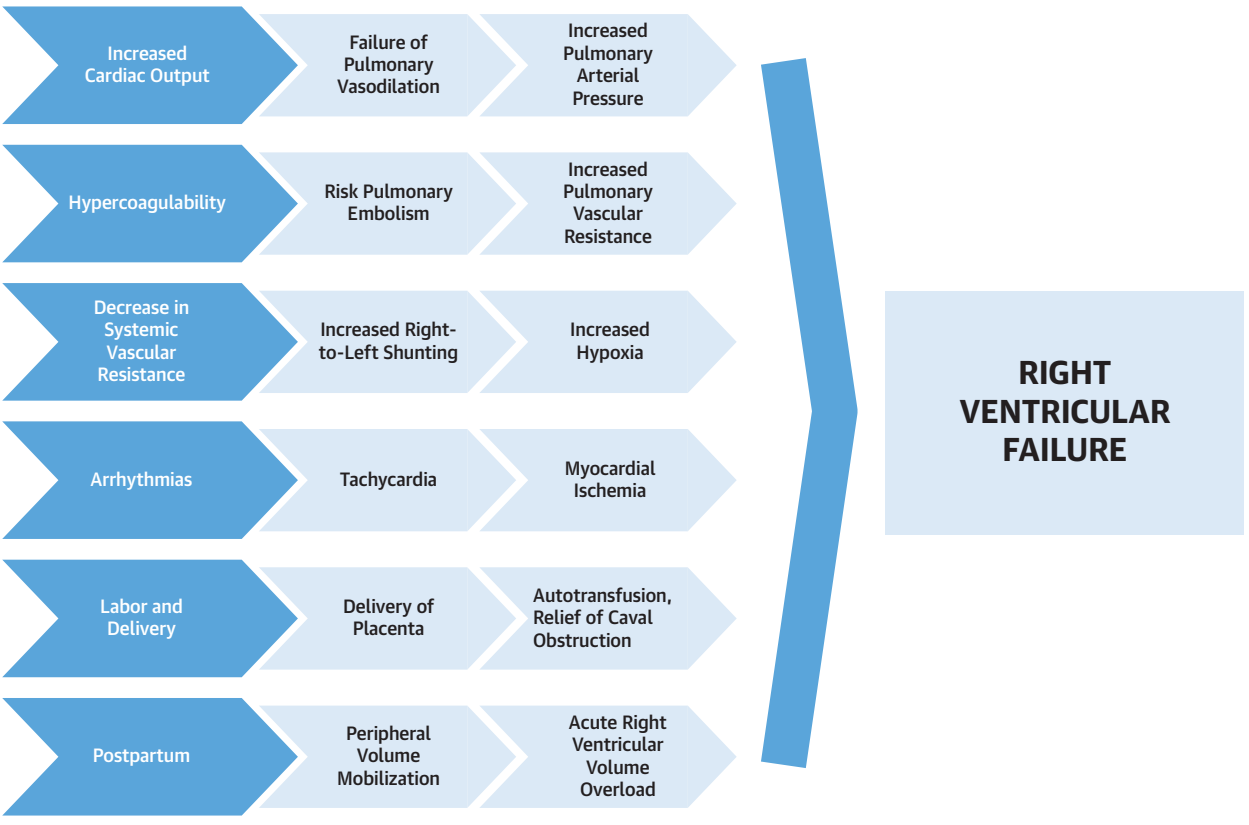
(2,23). Epidural anesthetic should be considered for all patients with CHD (2,23).

PULMONARY ARTERIAL HYPERTENSION

Pregnancy is associated with significant morbidity and mortality risk in all groups of pulmonary hypertension (37). Pulmonary arterial hypertension (PAH) is considered a contraindication for pregnancy by many U.S.-based and international guidelines (38,39). Serious cardiovascular complications may be precipitated by a variety of mechanisms during pregnancy, delivery, and the postpartum period, namely right heart failure (**Figure 4**) (40). Paradoxical emboli may occur in the presence of patent foramen ovale or Eisenmenger syndrome. Other serious complications include syncope and sudden cardiac death (41).

PRE-CONCEPTION EVALUATION. Patients with PAH who are long-term responders to calcium-channel blockers are a select group with the most favorable overall prognosis (37,42). Although some contemporary series have reported better outcomes, perhaps due to more widespread use of pulmonary vasodilators, maternal mortality and acute decompensation requiring urgent heart-lung transplantation continue to be reported (43–45). Each patient should be individually evaluated, with the risk-benefit ratio discussed, understanding the limits to our current knowledge. Pre-pregnancy right ventricular

FIGURE 4 Contributors to Pregnancy-Associated Right Heart Failure in Women With Pulmonary Hypertension



Maternal cardiovascular morbidity and mortality due to pulmonary arterial hypertension is most often related to the precipitation of right ventricular failure. Numerous physiological changes in pregnancy and the postpartum period predispose to right heart failure, including tachycardia, volume overload, hypoxia and hypercoagulability.

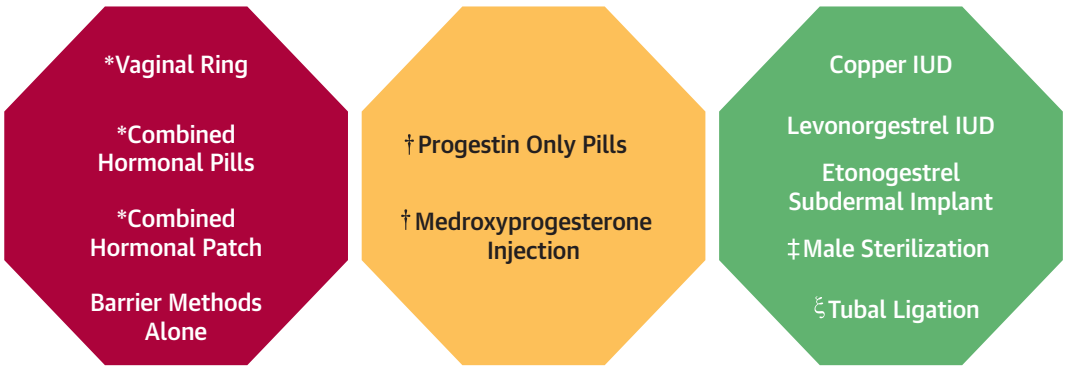
dysfunction, impaired hemodynamics, and poor functional class indicate high risk. Based on the risk-benefit ratio, current society guidelines recommend that women with PAH should be counseled that pregnancy is contraindicated, and highly effective contraception recommended (42,46).

CONTRACEPTION AND FERTILITY THERAPY. Contraception is discussed in detail in Part 5 of this series. Highly effective contraception should be considered in patients with PAH. Combined hormonal methods are generally considered contraindicated due to the risk of thromboembolism (25,46). The intrauterine device and subdermal implant are safe and provide superior efficacy (**Figure 5**). Bosentan may reduce the efficacy of oral contraceptive agents. Bosentan, ambrisentan, macitentan, and riociguat are all potentially teratogenic; if these are prescribed in women of childbearing age, dual mechanical barrier contraceptive techniques are recommended (46).

The safety of fertility procedures/therapies in patients with PAH is not known. Elective oocyte retrieval procedures for surrogacy are a risk, but can be considered in a PAH/CHD center with the appropriate multidisciplinary planning. Currently, no guidelines address the risks associated with fertility procedures or therapies.

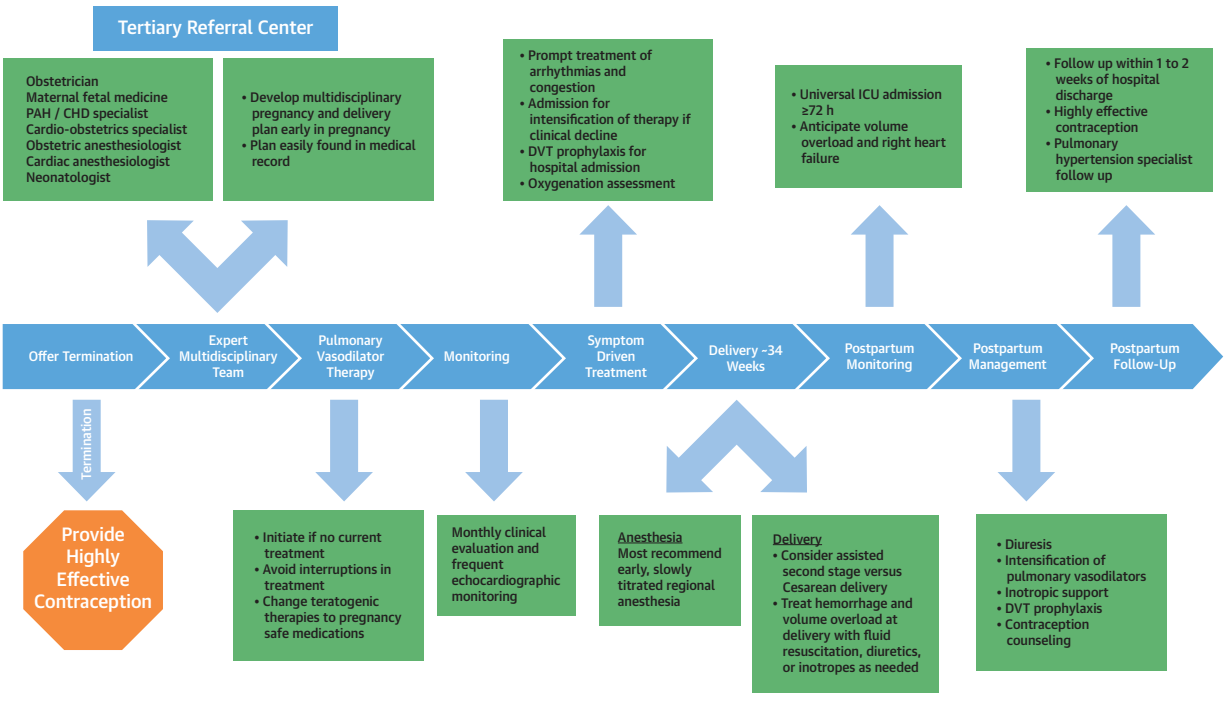
PREGNANCY MANAGEMENT. Pregnant women with PAH must be informed of the high risk of the pregnancy to both herself and the fetus, and pregnancy termination should be discussed (42,46). If termination is pursued, this should be performed in a hospital setting at a center with experience in the management of pulmonary hypertension. If pregnancy is continued, disease-targeted therapies should continue with a planned elective delivery and close multidisciplinary collaboration between obstetricians and the PAH team (**Figure 6, Table 3**) (42,46). Patients may need the addition of infusion therapy to baseline

FIGURE 5 Contraception Recommendations for Women With Pulmonary Hypertension



Highly effective contraception is recommended to prevent pregnancy in women with pulmonary hypertension. Although progestin-only pills and medroxyprogesterone acetate injection are safe, they are less effective than the long acting reversible and permanent contraceptive options. *Increased risk of complications related to thromboembolism. However, combined hormonal methods are still lower risk than pregnancy, so always weigh risk/benefit ratio and establish another highly effective method of contraception before stopping. †Safe but reduce efficacy (failure rate 6% to 12% per year). ‡Requires monogamous relationship. §Consider risks of laparoscopy for procedure if elective. IUD = intrauterine device.

FIGURE 6 Algorithm for the Management of Pregnancy in Women With Pulmonary Hypertension



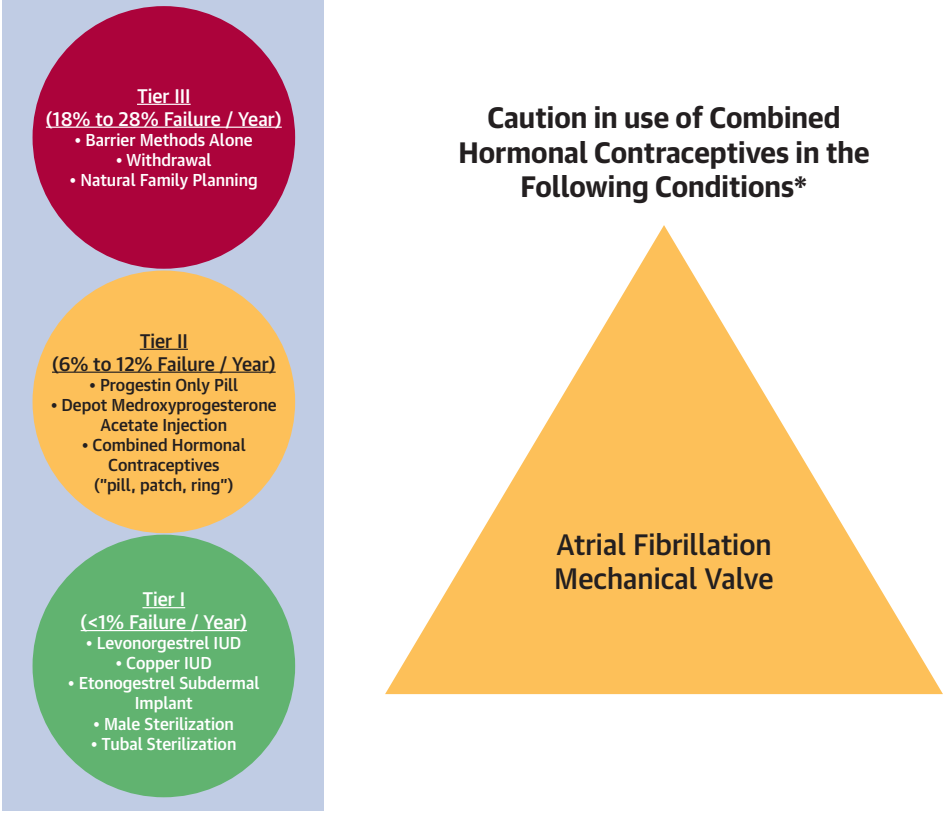
Management of pregnancy in a woman with pulmonary arterial hypertension requires meticulous multidisciplinary collaboration in a center experienced in managing pregnancy in this population of patients. Close monitoring before, during, and after delivery is essential to reduce adverse maternal events. DVT = deep vein thrombosis; ICU = intensive care unit.

TABLE 3 Pulmonary Vasodilator Therapy Safety in Pregnancy and Lactation

Medication	Pregnancy	Lactation
Ambrisentan	CONTRAINDICATED	Benefit/risk discussion with patient, no human data available
Bosentan	CONTRAINDICATED	Benefit/risk discussion with patient, no human data available
Epoprostenol	Benefit outweighs risk	Safe
Iloprost	Benefit outweighs risk	Benefit/risk discussion with patient, no human data available
Macitentan	CONTRAINDICATED	Benefit/risk discussion with patient, no human data available
Nitric oxide	Benefit outweighs risk	Benefit/risk discussion with patient, no human data available
Riociguat	CONTRAINDICATED	Benefit/risk discussion with patient, no human data available
Selexipag	Benefit/risk discussion with patient No human data available, but no risk of fetal harm in animal studies at 50x MRHD	Benefit/risk discussion with patient, no human data available
Sildenafil	Benefit outweighs risk	Benefit/risk discussion with patient, limited human data available, though harm not expected based on drug properties
Tadalafil	Benefit outweighs risk	Benefit/risk discussion with patient, no human data available
Treprostinil	Benefit outweighs risk	Safe

MRHD = maximum recommended human dose.

FIGURE 7 Contraception Recommendations for Women With Valvular Heart Disease



Long-acting reversible contraceptives (the IUD and subdermal implant) and permanent sterilization are safe and highly effective for all women with valvular heart disease. Caution should be advised when prescribing combined hormonal contraceptives to women with mechanical valves or atrial fibrillation due to the increased risk of thromboembolism. *Remember that combined hormonal contraceptives are still lower risk than pregnancy, so always weigh risk/benefit ratio and establish another highly effective method of contraception before stopping. IUD = intrauterine device.

TABLE 4 Pregnancy Risk Stratification and Management of Native Valvular Conditions

Valve Lesion	Common Underlying Conditions	WHO Risk	Potential Complications
Aortic stenosis	Bicuspid valve, subaortic membrane, supravalvular stenosis, rheumatic	II: mild III: moderate IV: AVA <1.0, peak gradient >50 mmHg	Arrhythmias, heart failure, aortic dissection if bicuspid aortopathy, urgent surgery, rarely death in WHO IV
Mitral stenosis	Congenital—parachute, rheumatic	III: mild MS IV: MVA <1.5 cm^2	Arrhythmias, thromboembolism, heart failure, urgent surgery or valvuloplasty, death in WHO IV
Aortic regurgitation	Bicuspid valve, aortopathy, history of Ross procedure, endocarditis, D-TGA with arterial switch, rheumatic	II: mild to moderate III: moderate to severe	Arrhythmias, heart failure, urgent surgery
Mitral regurgitation	Mitral valve prolapse, rheumatic, congenital—parachute, functional	II: mild III: moderate to severe	Arrhythmias, heart failure, worsening mitral regurgitation
Pulmonary stenosis	Congenital pulmonary stenosis, sequelae of tetralogy of Fallot	I: mild II: moderate III: severe	Arrhythmias, right heart failure, increased valve gradients
Pulmonary regurgitation	Congenital pulmonary stenosis - following valvuloplasty or valvotomy, sequelae of tetralogy of Fallot	I: mild to moderate II to III: severe	Arrhythmias, right heart failure
Tricuspid regurgitation	Ebstein anomaly, endocarditis, functional	I: mild II: moderate III: severe	Arrhythmias, right heart failure

While each patient requires individualized management, this table provides general disease-specific recommendation for the management of women with native valvular heart disease.

AS = aortic stenosis; AVA = aortic valve area; LA = left atrium; LAVI = left atrial volume index; MS = mitral stenosis; MVA = mitral valve area; PS = pulmonary stenosis; TR = tricuspid regurgitation; other abbreviations as in Table 2.

Continued on the next page

oral therapies for improved hemodynamic management. Hospitalization during the second trimester may be required due to the increased risk of premature labor and hemodynamic compromise (47). Anticoagulation should be continued for patients with a history of thromboembolism prior to pregnancy. Anticoagulation as long-term therapy for prevention of thromboembolism should be individualized (48).

DELIVERY PLANNING. A multidisciplinary approach to delivery at a pulmonary hypertension center including both the obstetric and cardiovascular anesthesiology services is recommended (49). It is best to have a comprehensive plan and a nonemergent procedure (43). There are no guidelines regarding the best method of delivery or anesthesia, and the delivery plan should be individualized for each patient. Some experts recommend early Cesarean delivery around 34 weeks gestation (48). A small series from the United Kingdom reported success in 10 pregnancies utilizing a tailored multiprofessional approach with early induction of targeted therapy, early planned delivery, and regional anesthetic techniques (50). Single-dose spinal anesthesia should be avoided due to the risk of hypotension and hemodynamic instability (48). In patients with Eisenmenger syndrome, recommendations for management of shunt lesions should be considered in addition to those for PAH (**Table 2**).

TABLE 4 Continued

Valve Lesion	Principles of Management	Delivery	Postpartum
Aortic stenosis	Multidisciplinary team for ≥ moderate AS	Consider assisted second stage or Cesarean if severe or symptomatic	Anticipate need for diuresis
	Consider pre-conception exercise testing in asymptomatic women	Slow titration of regional anesthesia	Consider monitoring ≥72 h
	Serial echocardiography for ≥ moderate AS	Avoid volume overload	
	Volume management with diuresis		
	Heart rate control		
	Prompt treatment of arrhythmias		
Mitral stenosis	Multidisciplinary team	Consider assisted second stage or Cesarean if ≥moderate or symptomatic	Anticipate need for diuresis
	Serial echocardiography	Slow titration of regional anesthesia	Consider monitoring ≥72 h
	Volume management with diuresis	Avoid volume overload	
	Heart rate control		
	Prompt treatment of arrhythmias		
	Anticoagulation for atrial fibrillation, left atrial thrombosis, prior embolism, severe MS, spontaneous echo contrast in the LA, LAVI ≥60 ml/m^2, or heart failure		
Aortic regurgitation	Volume management with diuresis	Vaginal delivery	Anticipate need for diuresis if ≥moderate
	Management of hypertension	Epidural recommended	
	Serial echocardiography if moderate to severe	Avoid volume overload	
Mitral regurgitation	Volume management with diuresis	Vaginal delivery	Anticipate need for diuresis if ≥moderate
	Management of hypertension	Epidural recommended	
	Serial echocardiography if moderate to severe	Avoid volume overload	
Pulmonary stenosis	Serial echocardiography for ≥ moderate PS	Vaginal delivery	Anticipate need for diuresis if ≥moderate
	Volume management with diuresis	Slow titration of regional anesthesia	
		Pre-load dependent	
Pulmonary regurgitation	Serial echocardiography for ≥ moderate PI or RV enlargement or dysfunction	Vaginal delivery	Anticipate need for diuresis if RV dysfunction is present
	Volume management with diuresis	Epidural recommended	
Tricuspid regurgitation	Serial echocardiography for ≥moderate TR or RV enlargement or dysfunction	Vaginal delivery	Anticipate need for diuresis if RV dysfunction is present
	Volume management with diuresis	Epidural recommended	

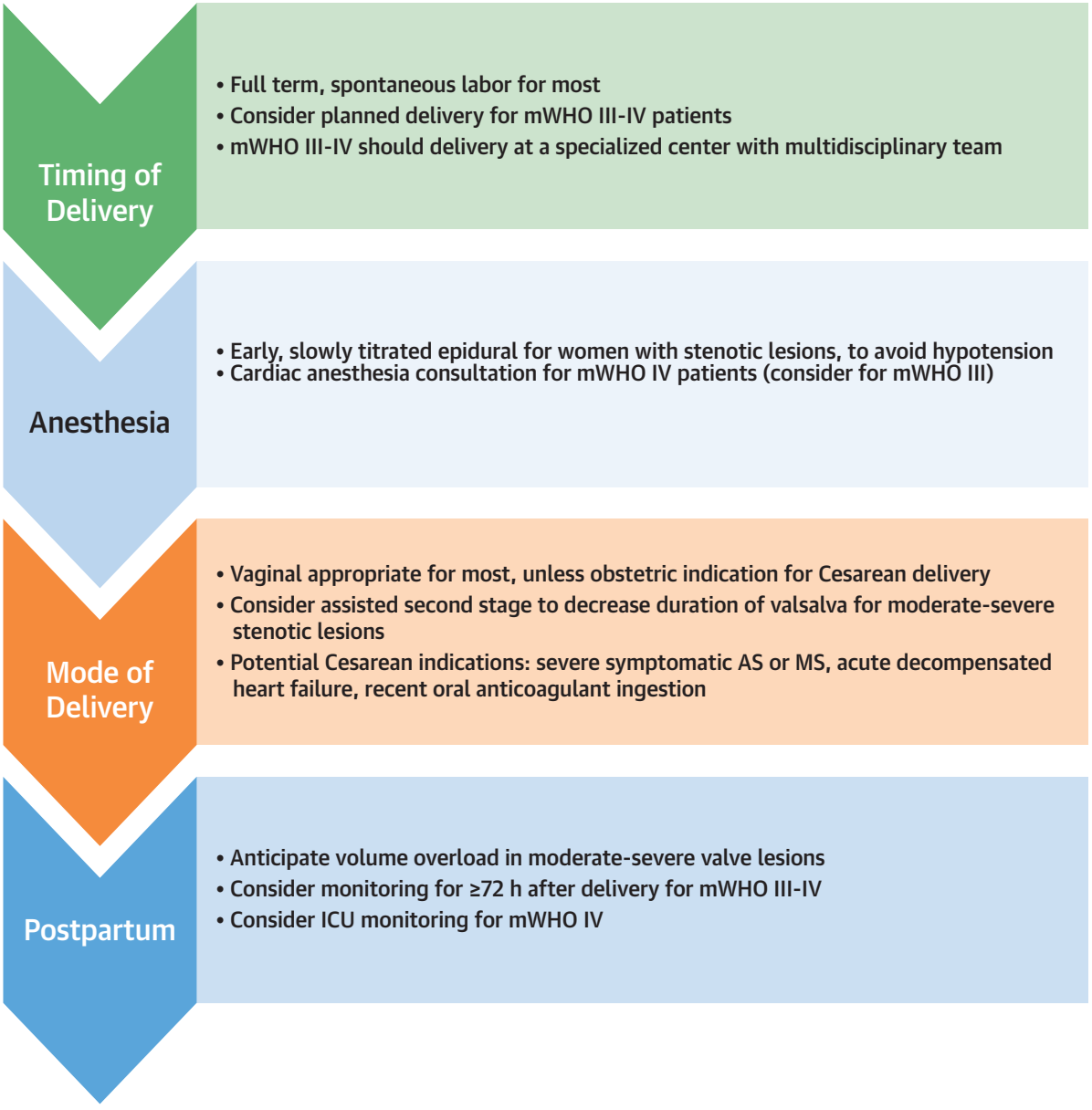
POSTPARTUM CARE. Most maternal deaths due to PAH occur in the first month postpartum, due to right heart failure, sudden death, or thromboembolism (48). Women with PAH should be monitored closely after delivery for evidence of right heart failure, and in an intensive care setting for at least the first several days due to the risk of rapid decompensation in the setting of postpartum volume shifts (48). Pharmacological thromboembolism prophylaxis in the postpartum period is essential (48).

VALVULAR HEART DISEASE

Valve disease among childbearing women in the United States is most frequently congenital, but rheumatic disease is more prevalent among patients who have emigrated from low-resource countries. Women with valvular heart disease are at increased risk for complications during pregnancy including heart failure, atrial arrhythmias, postpartum hemorrhage, and poor fetal outcomes (51).

PRE-CONCEPTION EVALUATION. Pre-conception risk stratification by a cardiologist and maternal fetal medicine specialist with expertise in valvular heart disease in pregnancy is recommended based upon functional class and echocardiography for all valvular conditions (52). Asymptomatic women with severe valve disease may be considered for risk assessment via exercise testing (52). Pre-conception valve intervention is recommended for women who meet guideline-based criteria for valve intervention, or who are modified World Health Organization IV pregnancy risk due to their valve condition (52).

FIGURE 8 Delivery Planning in Women With Valvular Heart Disease

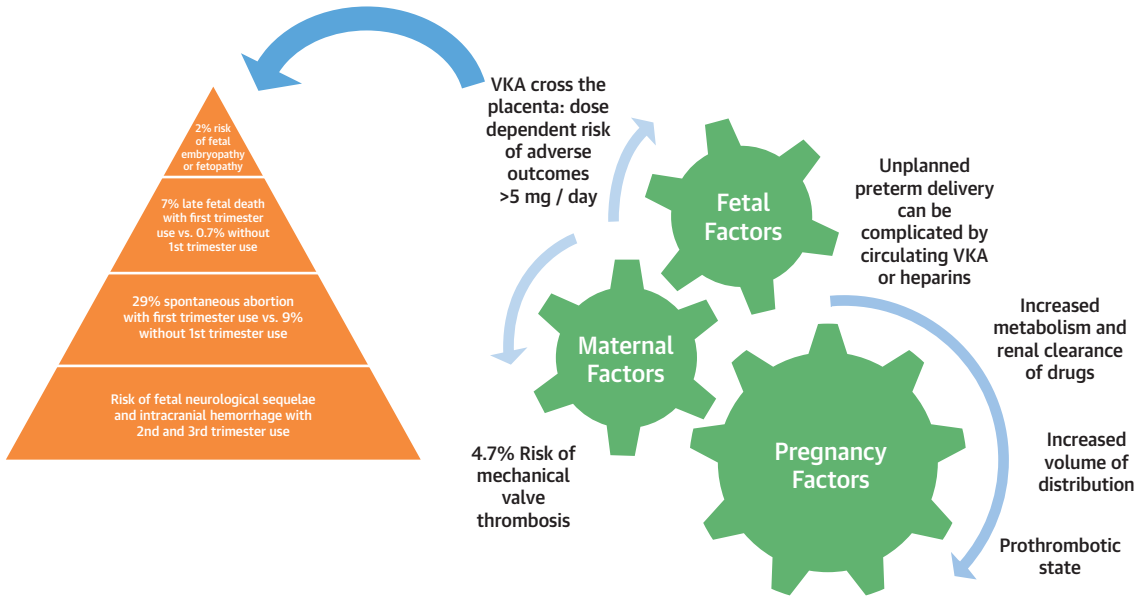


The multidisciplinary cardio-obstetrics team should collaborate to develop a delivery plan for women with mWHO class III to IV conditions. The delivery plan should include recommendations for anesthesia, monitoring, and timing/mode of delivery. Extended postpartum monitoring should be considered for women with ≥ moderate valve lesions due to the increased risk of postpartum heart failure. AS = aortic stenosis; ICU = intensive care unit; MS = mitral stenosis; mWHO = modified World Health Organization.

CONTRACEPTION. All methods of contraception are safe for women with uncomplicated valvular heart disease (25). Women with prosthetic heart valves or risk for thrombotic complications should be advised to avoid combined hormonal contraceptives due to the risk of thromboembolism, particularly if effective alternative options are available (**Figure 7**) (25).

PREGNANCY AND DELIVERY PLANNING. Women with severe valve disease (stages C and D) require an experienced multidisciplinary cardio-obstetrics team, including cardiologists with expertise in pregnancy for women with CHD or valvular heart conditions, maternal fetal medicine specialists, surgeons, and cardiac and obstetric anesthesiologists at a tertiary-

FIGURE 9 Maternal and Fetal Factors to Consider in the Management of Prosthetic Valves in Pregnant Women



Maternal physiological changes must be considered in addition to fetal risks of warfarin exposure when considering optimal medication choice and dosing for women requiring anticoagulation during pregnancy. VKA = vitamin K antagonists.

care center (52). The cardio-obstetrics team should develop a comprehensive pregnancy management and delivery plan according to the patient's individualized needs (**Table 4**) (4). The delivery plan, including the potential need for invasive hemodynamic monitoring, should be documented in the medical record prior to labor. Most asymptomatic women may be permitted to go into spontaneous labor (**Figure 8**). At the time of delivery, there is an abrupt increase in left ventricular afterload increasing the risk for acute heart failure. The early postpartum period is the highest risk time for deterioration, so extended inpatient observation and close outpatient follow-up are required.

SPECIFIC DISORDERS

BIOPROSTHETIC VALVES. It is uncertain whether pregnancy contributes to premature structural valve deterioration of bioprosthetic valves (53). Valves in

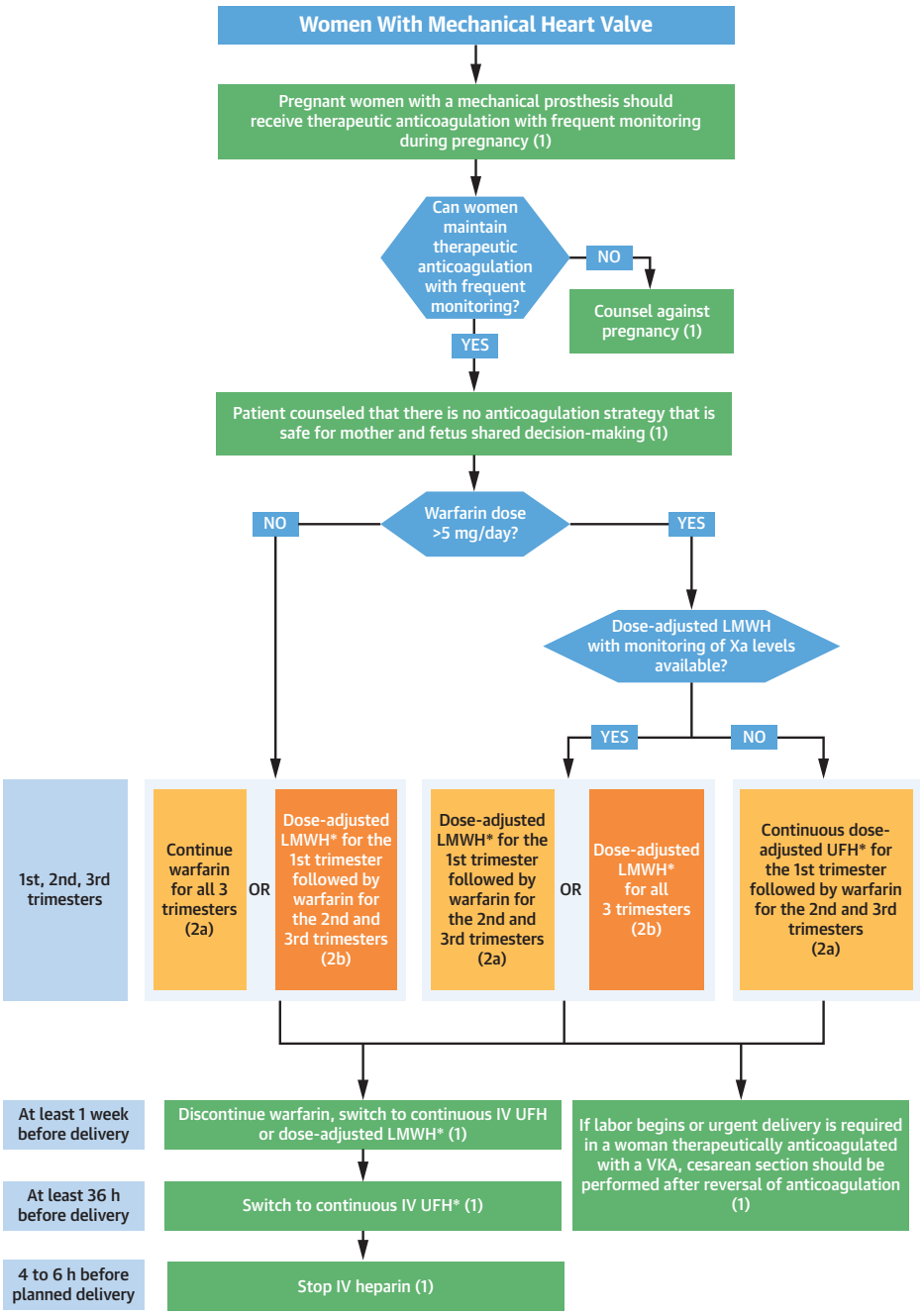
TABLE 5 Maternal and Fetal Risks of Pregnancy With Mechanical Heart Valves

	ROPAC		
	Mechanical Heart Valve	Bioprosthetic Heart Valve	No Prosthetic Valve
Maternal mortality	1.4	1.5	0.2
Any serious adverse event	42.0	21.0	22.0

	D'Souza et al. (55)			
	VKA Throughout	Heparins First Trimester/ VKA Second and Third Trimester	LMWH Throughout	UFH Throughout
Maternal mortality	0.9	2.0	2.9	3.4
Thromboembolism	2.7	5.8	8.7	11.2
Live births	64.5	79.9	92.0	69.5
Warfarin embryopathy or fetopathy	2.0	1.4	NA	NA

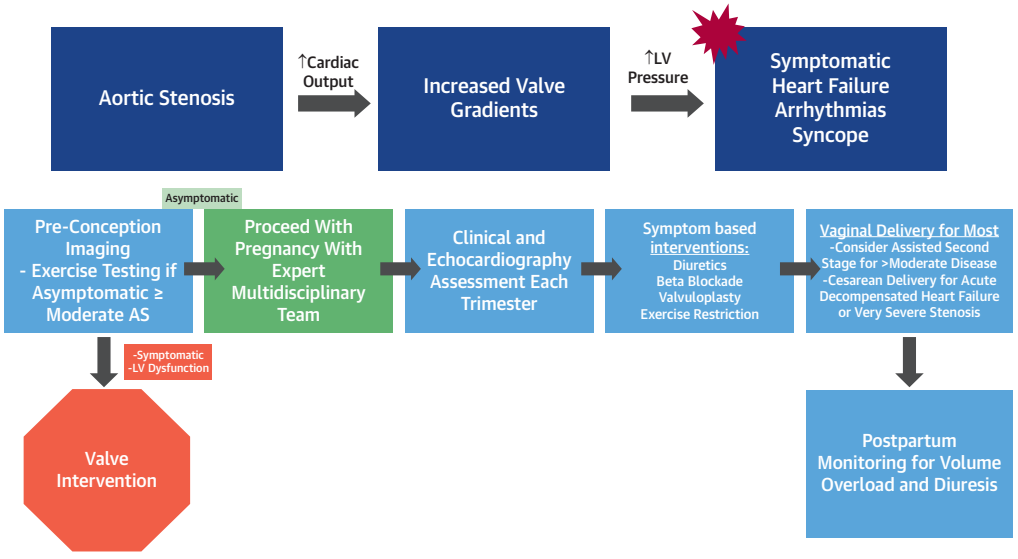
Values are %.
LMWH = low molecular weight heparin; NA = not applicable; UFH = unfractionated heparin; VKA = vitamin K antagonist.

FIGURE 10 **Management Algorithm for Pregnant Women With Mechanical Heart Valves**



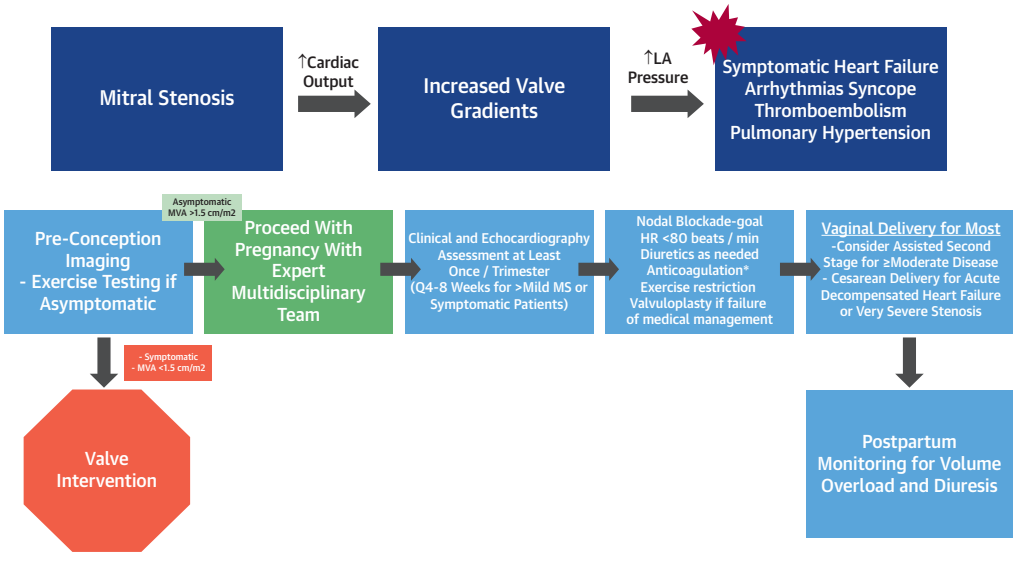
Reproduced from the 2020 American College of Cardiology/American Heart Association Valvular Heart Disease Guidelines. Shared decision making should be employed to determine the optimal anticoagulant dosing regimen for each individual patient during pregnancy. Weekly INR or Xa levels should be monitored to ensure adequate anticoagulation. Warfarin and LMWH need to be discontinued in advance of delivery, with an intravenous UFH bridge to permit for regional anesthesia. *Dose-adjusted LMWH should be given at least 2 times per day, with close monitoring of anti-Xa levels. Target to Xa level of 0.8 to 1.2 U/ml, 4 to 6 h after dose. Trough levels may aid in maintaining the patient in therapeutic range. Continuous UFH should be adjusted to aPTT 2 times control. **Green** = Class 1 recommendation; **yellow** = Class 2a recommendation; **orange** = Class 2b recommendation. aPTT = activated partial thromboplastin time; INR = international normalized ratio; LMWH = low molecular weight heparin; UFH = unfractionated heparin.

FIGURE 11 **Hemodynamic Changes and Proposed Management Algorithm for Pregnant Women With Aortic Stenosis**



Aortic valve gradients are expected to increase in the setting of pregnancy, and may lead to adverse maternal outcomes. Serial imaging, heart rate control, and volume management are useful in caring for pregnant women with MS. Although most women may undergo vaginal delivery, some may need consideration of assisted second stage or Cesarean delivery depending on disease severity and clinical status. LV = left ventricular; MS = mitral stenosis.

FIGURE 12 **Hemodynamic Changes and Proposed Management Algorithm for Pregnant Women With Mitral Stenosis**



Mitral valve gradients are expected to increase in the setting of pregnancy, and may lead to adverse maternal outcomes. Serial imaging, heart rate control, volume management, and anticoagulation are useful in caring for pregnant women with MS. Although most women may undergo vaginal delivery, some may need consideration of assisted second stage or Cesarean delivery depending on disease severity and clinical status. *Anticoagulation is indicated for atrial fibrillation, left atrial thrombosis, prior embolism, severe MS, spontaneous echo contrast in the LA, LA volume index ≥60 ml/m^2, or heart failure. HR = heart rate; LA = left atrium/atrial; MS = mitral stenosis; MVA = mitral valve area.

the mitral position are more likely to undergo structural deterioration than those in the aortic position.

MECHANICAL VALVES. Management of pregnant women with mechanical heart valves requires a balance of the maternal risk of thromboembolic complications with the risk of fetal teratogenicity and loss (**Figure 9**). Recent reviews have better defined the maternal and fetal risks of pregnancy and anticoagulation in women with mechanical heart valves (**Table 5**) (54,55). Anticoagulation management requires a thoughtful, detailed discussion with the patient. Recent American College of Cardiology/American Heart Association management guidelines are presented in **Figure 10** (56). Following delivery, intravenous unfractionated heparin should be resumed ~6 h after vaginal delivery or 12 h after Cesarean delivery, depending on adequacy of hemostasis. Warfarin should be resumed prior to hospital discharge, with a low molecular weight heparin bridge, and continued through breastfeeding.

AORTIC AND MITRAL STENOSIS. Severe aortic stenosis and mitral stenosis (MS) are associated with a high risk of adverse events in pregnancy, though even mild MS may be poorly tolerated (26,57-61). Transvalvular gradients will increase with the increased heart rate and stroke volume of pregnancy, and may precipitate heart failure, arrhythmias, or pulmonary venous hypertension. Exercise testing is recommended in asymptomatic patients with stenotic valvular disease to evaluate the need for preconception intervention (**Figures 11 and 12**) (23,52).

Left-sided stenotic valve lesions require close multidisciplinary management by an experienced team, with prompt treatment of congestion and arrhythmias. Symptoms may begin to develop in the second trimester, and women remain at risk for heart failure into the postpartum period. Beta-blockers are recommended to decrease the transvalvular flow rate and gradient, with diuretic agents as needed for congestion, and anticoagulation when indicated (52,62). For progressive symptoms despite medical therapy, percutaneous balloon valvuloplasty may be considered with abdominal shielding by an experienced operator in appropriate patients, preferably in the second trimester. In most cases, congenital MS is not amenable to balloon valvuloplasty, highlighting the importance of accurate pre-conception valve characterization. If balloon valvuloplasty is contraindicated, surgical valve replacement should be considered after early Cesarean delivery.

AORTIC AND MITRAL REGURGITATION. Chronic aortic and mitral regurgitation are generally well tolerated, although women with severe mitral regurgitation are at risk of heart failure, particularly in the postpartum period in the setting of volume mobilization. Patients with baseline symptoms or left ventricular systolic dysfunction should undergo surgery prior to conception (63). Acute valve regurgitation remains a surgical emergency and must be dealt with accordingly even in pregnancy.

PULMONARY STENOSIS. Pulmonary stenosis even when severe is generally well-tolerated in pregnancy (64). Women with pulmonary stenosis typically do not require intervention prior to or during pregnancy; balloon valvuloplasty can be considered after the first trimester for severe symptoms refractory to medical therapy.

PULMONARY AND TRICUSPID REGURGITATION. Pulmonic and tricuspid regurgitation are usually associated with CHD. In the absence of preconception right heart failure, women typically do well throughout pregnancy. Patients with right-sided valve procedures are at risk for atrial arrhythmias and right-sided heart failure, and may require diuretic agents in the later stages of pregnancy and following delivery.

CONCLUSIONS

Most women with congenital and heritable cardiovascular conditions can have a successful pregnancy. This requires coordinated multidisciplinary care from the pre-conception through the postpartum period to optimize maternal and fetal outcomes. Women with moderate to complex conditions require expert cardio-obstetric management at referral centers.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Dr. Bairey Merz has served as a consultant for Abbott and Sanofi; and has served on the Board of Directors for iRhythm. Dr. Bello is supported by the National Institutes of Health/National Heart, Lung, and Blood Institute (K23 HL136853-03, R01 HL153382-01). Dr. Gomberg-Maitland has received research grant support to GWU-MFA from Acceleron, Bayer, Complexa, and United Therapeutics; and has served as a consultant for Actelion, Altavant, Acceleron, Bayer, Gilead, Insemed, Reata, and United Therapeutics. Dr. Park has served as a consultant for Abbott. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr. Kathryn J. Lindley, Cardiovascular Division, Department of Medicine, Washington University School of Medicine, 660 South Euclid Avenue, Box 6068, St. Louis, Missouri 63110, USA. E-mail: Kathryn.lindley@wustl.edu. Twitter: @DrKLindley.

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KEY WORDS aortopathy, cardio-obstetrics, congenital, pregnancy, pulmonary hypertension