Curr Treat Options Cardio Med (2018) 20: 66
DOI 10.1007/s11936-018-0657-4

Pregnancy and Cardiovascular Disease (N Scott, Section Editor)

Anesthetic Treatment of Cardiac Disease During Pregnancy

Kate M. Cohen, MD
Rebecca D. Minehart, MD, MSHPEd
Lisa R. Leffert, MD[*]

Address
[*]Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, 55 Fruit Street, Boston, MA, 02114, USA
Email: lleffert@partners.org

Published online: 18 July 2018

This article is part of the Topical Collection on *Pregnancy and Cardiovascular Disease*

Keywords Obstetric anesthesia · Cardiac disease · Valvular disease · Peripartum cardiomyopathy · Labor analgesia

Abstract

Purpose of review This review summarizes the pathophysiology, peripartum treatment, and anesthetic management of parturients with cardiac disease. Valvular disease, coronary disease, and cardiomyopathy are specifically addressed in the context of the normal physiologic changes of pregnancy. We offer recommendations for anesthetic approaches, hemodynamic goals with an emphasis on interdisciplinary planning between anesthesiologists, cardiologists, cardiothoracic surgeons, obstetricians, maternal fetal medicine specialists, and neonatologists.
Recent findings Vaginal delivery with neuraxial analgesia can be well tolerated by many pregnant patients with cardiac disease when coordinated by an interdisciplinary team of experts.
Summary Cardiac disease in pregnancy can present a significant challenge for the interdisciplinary care team. A detailed understanding of each patient's cardiac pathology and the physiologic changes of pregnancy are critical to ensure a safe and successful labor and delivery. Optimized medical therapy in the peripartum period and neuraxial anesthesia with the judicious use of vasoactive agents can be of great benefit for these parturients. As is generally the case, cesarean delivery should be primarily reserved for obstetric indications and maternal wellbeing, with careful consideration of the fetus to guide best practices.

Introduction

Pregnancy is associated with notable cardiovascular physiologic changes in maternal cardiac output (CO), systemic vascular resistance (SVR), stroke volume (SV), heart rate (HR), and other hemodynamic parameters (Table 1, Fig. 1). Underlying cardiac pathology can have a profound effect on maternal and neonatal outcome. Cardiac disease is the most common non-obstetric reason for maternal death in the USA and the UK [5, 6]. Many women with cardiovascular disease can benefit from peripartum analgesia and anesthesia to facilitate labor pain management and safe vaginal or cesarean delivery. This review will discuss the primary etiologies of cardiac disease in pregnancy, treatment modalities, and relevant anesthetic techniques. We emphasize interdisciplinary collaboration within a highly specialized team when planning for and managing these patients during pregnancy, labor and delivery, and postpartum.

Cardiovascular impact of neuraxial and general anesthesia

Understanding and communicating about the basic principles of neuraxial and general anesthesia are key to understanding the impact of these techniques on parturients with cardiac disease.

Neuraxial anesthesia—which includes epidural and combined spinal epidural (CSE)—has been shown to provide safe and superior labor pain relief compared to intravenous or intramuscular opioids [7] and inhaled nitrous oxide [8]. This, in turn, decreases maternal circulating catecholamines. Neuraxial local anesthetic administration, whether as a bolus dose or a continuous-infusion via a catheter, results in a partial sympathectomy causing a decrease in systemic vascular resistance (SVR). There are also HR effects after neuraxial anesthesia placement related to the sympathectomy and cardiac reflexes. HR responses vary and should be monitored. Parturients demonstrate increased sensitivity to local

Table 1. Hemodynamic changes of pregnancy

Cardiovascular physiology of pregnancy	1st trimester	2nd trimester	3rd trimester	Overall change vs. baseline
Blood volume	Increase (sharp rise)	Increase	Increase	↑ 45%
Peripheral vascular resistance	Decrease	Decrease (lowest)	Plateau/slight increase	↓ 35–40%
Heart rate	Increase	Increase	Increase (maximum)	↑ 20–25%
Cardiac output	Increase (sharp rise)	Increase	Increase/decrease /plateau	Max ↑ 45%
Arterial pressure (systolic (SBP), diastolic (DBP), mean arterial pressure (MAP))	Decrease	Decrease (lowest)	Increase	SBP ↓ 6.2–7.2 mmHg DBP ↓ 4.5–8.9 mmHg MAP ↓ 5.4–9.8 mmHg
Left and right ventricular wall mass	Increase	Increase	Increase	LV ↑ 52% RV ↑ 40%
Left ventricular wall thickness	Increase	Increase	Increase	↑ 28%
Myocardial contractility and left and right ventricular ejection fraction	No change	No change	No change	–
Aortic augmentation index (stiffness)	Decrease	Decrease (lowest)	Increase	–
Factors I, II, V, VII, VIII, X, XII	Increase	Increase	Increase	–

[1–3]

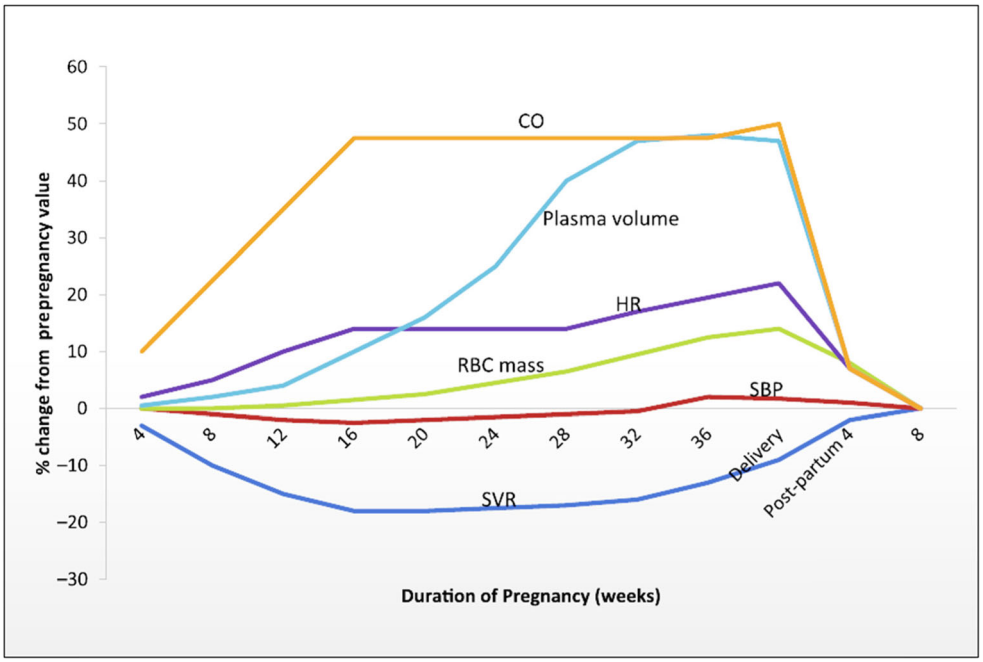

Fig. 1. Hemodynamic changes in pregnancy and postpartum. CO cardiac output, HR heart rate, RBC red blood cell, SBP systolic blood pressure, SVR systemic vascular resistance [4].

anesthetics. Neuraxial anesthetics appear to increase body temperature due to local anesthetic-mediated inflammatory mechanisms [9]. In some cases, this may further decrease SVR, increase HR, and decrease blood pressure.

When neuraxial techniques are unsuccessful or contraindicated and a surgical delivery is necessitated, then general anesthesia must be administered. Airway instrumentation can be challenging in the parturient due to increased oropharyngeal tissue edema, redundant soft tissue of the neck and chest, and risk of aspiration. A sympathetic surge may occur in response to direct laryngoscopy. Pretreatment with intravenous short-acting beta-blockers, lidocaine, or opioids can minimize this response. Propofol, used as an IV anesthetic induction agent, is a cardiac depressant; other IV anesthetic inductions agents such as etomidate and ketamine may better preserve cardiac function and may be preferential in certain circumstances. Inhalational agents are also negative inotropes and simultaneously decrease uterine tone, which can predispose the parturient to more blood loss. Both IV and inhaled anesthetics decrease SVR. General anesthesia leads to a decrease in blood pressure that is routinely augmented with vasopressor infusion. Parturients have a decrease in the minimum alveolar concentration (MAC) of general anesthesia; however, they are also particularly vulnerable to unintentional awareness under general anesthesia and therefore adequate amnestic agents must be used.

Valvular disease

Background: aortic stenosis

Valvular disease in the parturient may predate pregnancy but may be discovered for the first time during pregnancy. Diagnosing and treating a valvular lesion is an especially critical part of prenatal care, as the cardiovascular demands of pregnancy may rapidly shift the balance between well-compensated valvular disease and cardiovascular collapse, resulting in maternal and fetal compromise.

Symptomatic aortic valve (AV) stenosis in a woman of childbearing age is most commonly caused by the accelerated calcification of a congenital bicuspid valve [10]. AV stenosis is diagnosed and graded by echocardiography parameters (Table 2). AV stenosis becomes a fixed left ventricular outflow tract (LVOT) obstruction that, over time, causes the left ventricle (LV) to

Table 2. Grading criteria for aortic and mitral valve stenosis

Grading parameter	Mild stenosis	Moderate stenosis	Severe stenosis
Aortic Stenosis			
Aortic jet velocity (m/s)	2.6–2.9	3–4	> 4
Aortic mean gradient (mmHg)	< 20	20–40	> 40
Aortic valve area (cm^2)	> 1.5	1–1.5	< 1
Dimensionless index (VTI LVOT/VTI AV)	> 0.5	0.25–0.5	< 0.25
Mitral stenosis			
Valve area (cm^2)	> 1.5	1–1.5	> 1
Mitral mean gradient (mmHg)	< 5	5–10	> 10
Pulmonary arterial pressure (mmHg)	< 30	30–50	> 50

hypertrophy, stiffen, and eventually, fail. Hemodynamic goals for a patient with severe AV stenosis are to maintain a slow-normal heart rate to allow for adequate diastolic filling, sinus rhythm to preserve the contribution of atrial kick to cardiac output, afterload to promote coronary perfusion, and preload to support venous return to the heart.

Peripartum management: aortic valve stenosis

For patients with AV stenosis, the hemodynamic goals noted above may be achieved with a carefully titrated neuraxial anesthetic during labor. Neuraxial labor analgesia can provide a partial sympathetic block with decreased circulating catecholamine levels and can attenuate the intermittent elevation in material heart rate due to pain. A functional neuraxial labor analgesic also blunts the urge to bear down, thereby diminishing the change in preload caused by the Valsalva maneuver [11]. There can be perils to rapidly dosing a neuraxial anesthetic in patients with AV stenosis, as fast onset of profound sympathectomy reduces SVR and preload and results in compensatory tachycardia. Infusing phenylephrine, an alpha-1 adrenergic agonist, starting at 30–50 mcg/min after neuraxial placement, can maintain vascular tone and avoid major decreases in SVR and preload. Phenylephrine will also result in a helpful reflexive bradycardia. A recent meta-analysis suggests that healthy parturients receiving spinal anesthesia for cesarean delivery derive some hemodynamic benefit from a dose of IV ondansetron before neuraxial anesthesia. This administration presumably mitigates the Bezold-Jarish reflex because of the drug's action on 5HT3 receptors [12••]. It is possible that administration of ondansetron prior to labor analgesia will offset the drop in SVR as well. Invasive arterial blood pressure monitoring of patients with severe disease and associated remodeling of the myocardium, before the neuraxial anesthetic, may be beneficial.

Background: mitral stenosis

Mitral stenosis (MS) is the most poorly tolerated cardiac lesion in pregnancy. In the obstetric population, MS is typically caused by rheumatic disease. The diagnostic and grading criteria of MS are described in Table 2. MS causes the left atria to become enlarged. Patients are then susceptible to atrial tachycardias and thromboembolic events from dislodging atrial clots that developed due to stasis, the hypercoagulable state of pregnancy and nonlaminar flow. Pulmonary venous pressure increases due to back-flow of blood from the left atrium into the pulmonary artery leading to pulmonary arterial hypertension (PAH) and increased pulmonary venous resistance (PVR). These pathologic changes can ultimately cause pulmonary edema and right ventricular failure.

Peripartum management: mitral stenosis

Hemodynamic goals for parturients with MS are to (1) maintain a slow heart rate to minimize the transvalvular gradient and (2) maintain or restore sinus rhythm in order to preserve the atrial kick needed for adequate left ventricular end-diastolic volume (LVEDV). Avoiding

factors that increase pulmonary artery (PA) pressures—hypoxia, hypercarbia, acidosis, and pain—is also critical. If severe MS is diagnosed before pregnancy, then the ideal preconception procedure is a percutaneous valvolplasty if technically feasible. This approach avoids the need for long-term anticoagulation associated with a mechanical valve replacement. If severe MS is diagnosed during pregnancy, it is preferable to wait until the second trimester for a percutaneous valvuloplasty to avoid radiation exposure to the fetus during organogenesis. As cardiopulmonary bypass carries a significant risk of fetal demise, open heart surgery is avoided whenever possible [13].

Medical therapy for patients with MS includes anticoagulation in the presence of atrial fibrillation and beta blockade [14–17]. Maternal heart rate control is critical even if the patient remains in sinus rhythm. Tachycardia increases the trans-mitral gradient and incidence of pulmonary edema [18]. Atrial fibrillation (AF) must be aggressively treated with antiarrhythmic agents, or in the hemodynamically unstable patient, with cardioversion, to reestablish sinus rhythm. Active management of fluid status of MS patients should be done with careful monitoring of input and output and judicious use of diuretics, specifically hydrochlorothiazide, triamterene, or amiloride [19]. Severely affected patients may not tolerate the increased blood volume of the second and third trimester when coupled with the associated increased heart rate of exertion.

Neuraxial labor analgesia can be particularly beneficial for the peripartum management of obstetric patients with moderate or severe MS. Providing excellent labor analgesia can minimize pain-induced tachycardia that can cause sudden pulmonary edema from an overloaded left atrium massive increase in interstitial fluid and hydrostatic imbalance in the pulmonary capillaries. Inhaled nitrous oxide (N_2O) is relatively contraindicated in patients with MS, as N_2O can directly increase peripheral vascular resistance (PVR) and reduce the FiO2, secondarily increasing PVR. Pulmonary artery catheters are typically reserved for only the most severe cases given their associated complications (right bundle branch block, tricuspid valve damage or pulmonary artery rupture) and logistical hazards. Transthoracic echocardiography (TTE) is increasingly employed in the obstetric setting to monitor biventricular function and PA pressures.

As with AV stenosis, a well-working neuraxial labor analgesic blunts the urge to bear down, and therefore, diminishes the alteration in preload caused by the Valsalva maneuver which increases SVR and PVR [11]. Allowing passive fetal descent with uterine contractions and gravity, followed by a forceps- or vacuum-assisted vaginal delivery may be beneficial if the patient cannot physiologically tolerate Valsalva. In these cases, a slowly titrated dose of concentrated local anesthetic, such as 5–8 ml of 3% 2-chloroprocaine or 2% lidocaine, can provide adequate perineal relaxation and maternal comfort. The parturient may need additional medication for perineal repair. If the patient has sustained a high degree perineal laceration, she may benefit from a dose of long-acting neuraxial opioid, such as 2–3 mg preservative-free morphine administered epidurally, for postpartum analgesia.

The most vulnerable time for maternal pulmonary edema is immediately after delivery. Acute relief of aortocaval compression associated with delivery of the fetus and autotransfusion from the contracting uterus increases preload by approximately 30% [20]. This redistribution of intravascular volume coupled with an increase in heart rate increases the already elevated trans-mitral gradient leading to elevated PA pressures and pulmonary edema. Prophylactic diuretic dosing and oxygen supplementation may mitigate these effects.

Similarly, postpartum hemorrhage with its associated abrupt decrease in filling may also be poorly tolerated. As such, availability of ICU level care is important considerations to plan for ahead of time.

Background/peripartum management: pulmonic stenosis

Pulmonic stenosis (PS) can be an isolated congenital valvular lesion or can be among a constellation of congenital abnormalities, like in tetralogy of Fallot (TOF). Affected women generally have a normal cardiopulmonary function during pregnancy and delivery if PS is an isolated defect. Patients with PS may experience higher rates of pre-eclampsia and thromboembolic events, which have implications for anticoagulation and timing of neuraxial anesthesia placement [21]. Percutaneous valvuloplasty can be performed if the PS is severe and leads to right heart failure, for example, during the blood volume expansion in the second trimester.

Background: mitral and aortic insufficiency

Chronic regurgitant valvular disease, caused by an incompetent mitral or aortic valve, is generally well tolerated during pregnancy. Mitral regurgitation (MR) is most frequently caused by MV prolapse in the

developed countries, but worldwide the most common cause is rheumatic disease [22]. The regurgitant fraction from the LV to the LA may comprise a large percentage of the ejection fraction and detract from forward flow of blood to the aorta. MR causes left-sided volume overload that can lead to left atrial enlargement, increased left ventricular wall hypertrophy, and eventually LV failure. Aortic insufficiency (AI) is seen with a bicuspid valve, rheumatic valve, connective tissue disease, or dilated ascending aorta with annular dilation [22]. Aortic insufficiency overloads the LV during diastole, with blood entering anterograde through the mitral valve and retrograde through the aortic valve. Both EDV and ESV increase, as does stroke volume and left ventricular wall pressure. In response, the LV hypertrophies, dilates, and eventually fails.

Peripartum management: mitral and aortic insufficiency

The hemodynamic goals of both MR and AI are to minimize regurgitant time by maintaining a high-normal heart rate, to optimize the transvalvular gradient by increasing preload and decreasing afterload, and to encourage forward flow and accommodate the larger stroke volume by preserving inotropy. The natural physiologic changes of pregnancy are aligned favorably with the hemodynamic goals of these regurgitant lesions. The development of placental vascular bed and high-progesterone state both decrease maternal SVR. Heart rate naturally increases as does the circulating blood volume. Treatment for the parturient is considered when left ventricular dysfunction develops. Therapy includes restricting activity, adhering to a low-sodium diet and initiating medical therapy for afterload reduction. ACE inhibitors and angiotensin II receptor blockers (ARBs) are a mainstay of therapy for a non-parturient, but they are teratogenic [23]. Instead, nitrates [24] and hydralazine are used for vasodilation in the parturient [25, 26]. Beta blockers and diuretics may be used with careful monitoring of maternal blood pressure and fluid status.

Acute MR and AI, from papillary rupture or dissection, can result in critical illness requiring immediate surgical intervention.

Background/peripartum management: tricuspid and pulmonic regurgitation

Tricuspid regurgitation (TR) is a normal physiologic development during pregnancy, whereas pulmonic regurgitation (PR) is most commonly seen in parturients who have had corrective interventions to a previously stenotic valve. In the absence of RV failure, TR and PR infrequently cause clinically significant developments. If they do become symptomatic, the physiologic manifestations of these valvular lesions are treatable with diuretics.

Myocardial infarction

Background: myocardial infarction

Myocardial infarction (MI) during pregnancy is not common [27–29]. Spontaneous coronary artery dissection (SCAD) is the most common etiology [29]. The physiologic changes in blood volume and cardiac output during pregnancy and delivery can magnify shear forces of the blood flowing through the coronary vessels, resulting in a greater propensity for dissection. SCAD typically occurs postpartum, within 6 weeks of delivery [30]. The pathophysiology may relate to hormonally mediated vascular changes, specifically to the high-progesterone state of pregnancy or to the postpartum estrogen withdrawal [31].

Peripartum management: myocardial infarction

If a patient is postpartum, then treatment of her MI is the same as for a non-obstetric patient. If she is pregnant at the time of her MI, then the fetal risks need to be considered, although the well-being of the mother typically prevails.

Therapy for treating SCAD is dependent on the timing and severity of the infarction. Medical therapy for SCAD includes aspirin and beta blockade. SCAD resulting in STEMI or hemodynamic instability should be evaluated by cardiac catheterization with the goals of improving myocardial perfusion. Percutaneous coronary intervention (PCI), unfortunately, has a low success rate and high probability of propagating existing or causing new dissections [32]. If the patient remains hemodynamically unstable after MI, then there should be an interdisciplinary discussion between cardiology, obstetric, and anesthesia experts about whether delivery of the baby is indicated.

During labor, patients with SCAD may benefit from an anesthetic plan that minimizes the change in vascular pressure over time. For a vaginal delivery, minimizing maternal pain and expulsive efforts with a dense

neuraxial anesthetic is likely to be beneficial. Reinforcement of the anesthetic with more concentrated local anesthetic (e.g., 2% lidocaine with epinephrine) may be prudent before low-forceps- or vacuum-assisted delivery. Diuretics just before the second stage of labor may offset the post-delivery increased filling (see the "Peripartum management: mitral stenosis" section).

If not needed for urgent intervention for maternal safety, ionizing radiation associated with PCI is ideally avoided in pregnant women order to minimize fetal risk. In addition, clopidogrel, typically used as part of dual antiplatelet therapy after stent placement, has unknown fetal effects. Similarly, CABG-associated cardiopulmonary bypass (CBP) carries a high risk of fetal demise. However, ultimately critical therapy for the mother should not be withheld out of concern for the fetus.

Heart failure

Background: peripartum cardiomyopathy

Peripartum cardiomyopathy (PPCM) is a rare disease, with an incidence of < 0.1%, which carries a significant morbidity and mortality [33–38] and is diagnosed based on the criteria delineated in Table 3 [39]. There is no consensus as to the etiology of PPCM, although there are multiple hypotheses [40–46]. PPCM can be a challenging diagnosis to make by history alone, because the symptoms of early heart failure are similar to those of late pregnancy—dyspnea, fatigue, and pedal edema. Transthoracic echocardiography (TTE) is a key diagnostic tool for revealing cardiac pathology. Cardiac MRI is an alternative diagnostic technique that employs non-ionizing radiation. Gadolinium is not typically used in the protocol because it crosses the placenta and has unknown fetal effects [47]. In a postpartum woman that does not recover full cardiac function, the rate of death from heart failure during or after the subsequent pregnancy is significantly higher than that of a woman who has fully recovered her cardiac function [48].

Peripartum management: peripartum cardiomyopathy

Patients with only a moderately depressed ejection fraction (EF) and compensated PPCM require minimal or no medical management beyond usual care for delivery. Parturients with decompensated heart failure require medical optimization with preload and afterload reduction. Nitrates and hydralazine are the mainstays of therapy. As an elevated heart rate can lead to arrhythmias and cardiac death, beta blocker therapy should be instituted. Beta-1 selective agents are preferred for antepartum compensated patients to avoid the unwanted beta-2 effects on uterine tone. ACE inhibitors are reserved for afterload reduction and neurohormonal modification after delivery because of their teratogenicity [49, 50]. Digoxin can safely be used in pregnant women to increase inotropy. For patients who are volume overloaded, low-sodium intake should be encouraged. Diuretics should be carefully titrated to preserve maternal perfusion of the placental vessels that lack auto-regulation.

Prolactin is thought to mediate the cellular mechanism of PPCM [51]. There is evidence to suggest that inhibiting prolactin improves myocardial PPCM [52, 53••, 54]. Bromocriptine, the dopamine-2D agonist of prolactin, has been used therapeutically. Side effects from it include increased thrombotic risk, reduced lactation, and hypoglycemia.

Women who are pregnant or newly postpartum with severe PPCM are at increased risk of forming intracardiac clots due to both heart failure and to pregnancy itself. This vulnerability can, in turn, increase the risk of systemic thromboembolism [55]. If a pregnant woman's EF is less than 30–35%, then she should be treated with low molecular weight heparin (LMWH) in the antepartum setting and warfarin in the postpartum setting [56••, 57]. Patients who have

Table 3. Diagnostic criteria for peripartum cardiomyopathy

First criteria	Echocardiographic evidence of new left ventricular systolic dysfunction developing in late pregnancy and up to 20 weeks (5 months) postpartum.
Second Criteria	Absence of an alternative cause of cardiac failure.
Third Criteria	LV EF less than 45%.

atrial fibrillation or a known mural thrombus should be considered for anticoagulation regardless of their EF. The duration of anticoagulation after delivery is dependent upon the rate of cardiac recovery.

As per usual, the method of fetal delivery should be based on obstetric indications with a preference for vaginal delivery unless otherwise indicated. Neuraxial analgesia for labor or cesarean delivery can be instrumental in decreasing circulating pain and catecholamine levels, reducing preload and afterload and minimizing post-delivery increases in cardiac output [58]. Optimal interdisciplinary planning, communication, and widespread availability of relevant protocols can greatly expedite management in parturients that are anticoagulated. The Society of Obstetric Anesthesia and Perinatology (SOAP) and American Society of Regional Anesthesia (ASRA) recommend that high-dose LMWH be held for 24 h prior to a neuraxial anesthetic procedure and 12 h for low dose LMWH, with tactics and decision aids to guide management and maximize the use of neuraxial anesthesia in both elective and non-elective settings [59, 60].

In patients who have decompensated PPCM, invasive monitoring and circulatory support may become necessary: arterial line for continuous monitoring of blood pressure and blood gas evaluation and central venous catheter for prolonged infusion of vasopressors. Echocardiography can be used to calculate cardiac output instead of the more invasive pulmonary artery (PA) catheter with its potential complications. Mild cases of hypoxia can be treated with CPAP, whereas endotracheal intubation and mechanical ventilation with PEEP may be needed for more severe hypoxia. ECMO can be considered for circulatory support as a bridge to recovery or to transplant.

Congenital heart disease

Background

Congenital heart disease has become more prevalent in parturients due to advances in surgery and medical therapy [61]. Corrected congenital heart disease is generally well tolerated during pregnancy often requiring routine labor and delivery care. Discussion of simple and complex congenital lesions is beyond the scope of this review. However, the patients who are of particular concern are those with chronic left to right shunting that progress to right-sided volume overload and pulmonary hypertension. Eventually, the elevated right-sided pressures cause reversal of the shunt, and deoxygenated blood enters the systemic circulation. This is called Eisenmenger's syndrome. It results in significant maternal and fetal consequences. Patients with severe pulmonary hypertension may be counseled to avoid pregnancy or undergo a first-trimester interruption of pregnancy, as the maternal mortality rate is over 30% [62].

Peripartum management

The maladaptation of Eisenmenger's syndrome is generally considered to be irreversible, but there are some medical therapies that can be used to optimize pregnant women for delivery [63]. Sildenafil, a cGMP-specific phosphodiesterase type 5 inhibitor, increases pulmonary blood flow and decreases hypoxia in patients with Eisenmenger's [64]. Data on its safety during pregnancy is still being evaluated. Sildenafil is also being investigated as treatment for placental insufficiency because it appears to also increase uterine blood flow by uterine vascular dilatation [65••]. Bosentan, a dual endothelial receptor antagonist, is known to cause fetal harm and should be avoided before delivery. Prophylactic anticoagulation with LMWH should be considered after 20 weeks gestation, given the hypercoagulable state of pregnancy and the potentially catastrophic effects of venous thromboembolism and right heart failure in these patients.

To support a parturient with Eisenmenger's syndrome in labor, central monitoring with an arterial line and central venous line is indicated. Intensive care nursing and physician specialists should be part of the interdisciplinary care team. Several aspects of labor and delivery, including the pain of contractions and Valsalva maneuvers, can exacerbate right-to-left shunting and worsen hypoxemia. Medical therapies should include oxygen face mask and inhaled nitric oxide or inhaled prostaglandins, like epoprostenol, if available. These inhaled agents have no known adverse effects on neonates [66]. Neuraxial anesthesia should be placed early in labor and dosed for a dense sensory block to abolish pain and diminish the urge to push. Consider practicing a loss of resistance to saline technique for the epidural procedure and de-airing both epidural and intravenous boluses to minimize the introduction of air bubbles. A low-forceps-assisted delivery can minimize maternal expulsive effort. Uterotonic agents that increase

intrapulmonary shunting, such as Hemabate (prostaglandin F2 alpha), should be avoided [67]. With increased chance of right-to-left intracardiac shunting, paradoxical embolus is possible; be prepared for decompensation at any time, particularly after delivery, necessitating urgent intubation or ECMO.

Conclusion

Cardiac disease in pregnancy can present a significant challenge for the interdisciplinary care team. A detailed understanding of each patient's cardiac pathology and the physiologic changes of pregnancy are critical to ensure a safe and successful labor and delivery. Optimized medical therapy in the peripartum period and neuraxial anesthesia with the judicious use of vasoactive agents can be of great benefit for these parturients. As is generally the case, cesarean delivery should be primarily reserved for obstetric indications and maternal well-being, with careful consideration of the fetus, should guide best practices.

Compliance with Ethical Standards

Conflict of Interest
The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:
•• Of major importance

1. Sanghavi M, Rutherford JD. Cardiovascular physiology of pregnancy. Circulation. 2014;130(12):1003–1008.
2. Foley M, Lockwood C, Gersh B, Eckler K. Maternal adaptations to pregnancy: cardiovascular and hemodynamic changes. UpToDate, 2017; https://www.uptodate.com/contents/maternaladaptations-to-pregnancy-cardiovascular-and-hemodynamic-changes.
3. Grindheim G, Estensen ME, Langesaeter E, Rosseland LA, Toska K. Changes in blood pressure during healthy pregnancy: a longitudinal cohort study. J Hypertens. 2012;30(2):342–350.
4. Bhatt AB, DeFaria Yeh D. Pregnancy and Adult Congenital heart disease. Cardiol Clin. 2015;33(4):611–23. ix. https://doi.org/10.1016/j.ccl.2015.07.008.
5. Creanga AA, Berg CJ, Ko JY, Farr SL, Tong VT, Bruce FC, et al. Maternal mortality and morbidity in the United States: where are we now? J. Women's Health (2002). 2014;23(1):3–9. https://doi.org/10.1089/jwh.2013.4617.
6. Knight MNM, Tuffnell D, Kenyon S, Shakespeare J, Brocklehurst P, Kurinczuk JJ (Eds.) on behalf of, MBRRACE-UK. Saving lives, improving mothers' care—surveillance of maternal deaths in the UK 2012–14 and lessons learned to inform maternity care from the UK and Ireland confidential enquiries into maternal deaths and morbidity 2009–14. University of Oxford, National Perinatal Epidemiology Unit: Oxford: 2016.
7. Anim-Somuah M, Smyth RM, Jones L. Epidural versus non-epidural or no analgesia in labour. Cochrane Database Syst Rev. 2011;12:Cd000331. https://doi.org/10.1002/14651858.CD000331.pub3.
8. Likis FE, Andrews JC, Collins MR, Lewis RM, Seroogy JJ, Starr SA, et al. Nitrous oxide for the management of labor pain: a systematic review. Anesth Analg. 2014;118(1):153–67. https://doi.org/10.1213/ANE.0b013e3182a7f73c.

9. Sultan P, David AL, Fernando R, Ackland GL. Inflammation and epidural-related maternal fever: proposed mechanisms. Anesth Analg. 2016;122(5):1546–53. https://doi.org/10.1213/ane.0000000000001195.
10. Beppu S, Suzuki S, Matsuda H, Ohmori F, Nagata S, Miyatake K. Rapidity of progression of aortic stenosis in patients with congenital bicuspid aortic valves. Am J Cardiol. 1993;71(4):322–7.
11. Gomar C, Errando CL. Neuroaxial anaesthesia in obstetrical patients with cardiac disease. Curr Opin Anaesthesiol. 2005;18(5):507–12. https://doi.org/10.1097/01.aco.0000183108.27297.3c.
12.•• Sahoo T, SenDasgupta C, Goswami A, Hazra A. Reduction in spinal-induced hypotension with ondansetron in parturients undergoing caesarean section: a double-blind randomised, placebo-controlled study. Int J Obstet Anesth. 2012;21(1):24–8. https://doi.org/10.1016/j.ijoa.2011.08.002.

Early treatment with ondansetron before spinal anesthesia prevents hypotension.

13. Mahli A, Izdes S, Coskun D. Cardiac operations during pregnancy: review of factors influencing fetal outcome. Ann Thorac Surg. 2000;69(5):1622–6.
14. Hameed A, Akhter MW, Bitar F, Khan SA, Sarma R, Goodwin TM, et al. Left atrial thrombosis in pregnant women with mitral stenosis and sinus rhythm. Am J Obstet Gynecol. 2005;193(2):501–4. https://doi.org/10.1016/j.ajog.2005.01.027.
15. Steinberg ZL, Dominguez-Islas CP, Otto CM, Stout KK, Krieger EV. Maternal and fetal outcomes of anticoagulation in pregnant women with mechanical heart valves. J Am Coll Cardiol. 2017;69(22):2681–91. https://doi.org/10.1016/j.jacc.2017.03.605.
16. Barbour LA. Current concepts of anticoagulant therapy in pregnancy. Obstet Gynecol Clin N Am. 1997;24(3):499–521.
17. Dimitrakakis C, Papageorgiou P, Papageorgiou I, Antzaklis A, Sakarelou N, Michalas S. Absence of transplacental passage of the low molecular weight heparin enoxaparin. Haemostasis. 2000;30(5):243–8. https://doi.org/10.1159/000054140.
18. al Kasab SM, Sabag T, al Zaibag M, Awaad M, al Bitar I, Halim MA, et al. Beta-adrenergic receptor blockade in the management of pregnant women with mitral stenosis. Am J Obstet Gynecol. 1990;163(1 Pt 1):37–40.
19. Al-Balas M, Bozzo P, Einarson A. Use of diuretics during pregnancy. Can Fam Physician. 2009;55(1):44–5.
20. Ueland K, Gills RE, Hansen JM. Maternal cardiovascular dynamics. I. Cesarean section under subarachnoid block anesthesia. Am J Obstet Gynecol. 1968;100(1):42–54.
21. Drenthen W, Pieper PG, Roos-Hesselink JW, Schmidt AC, Mulder BJ, van Dijk AP, et al. Non-cardiac complications during pregnancy in women with isolated congenital pulmonary valvar stenosis. Heart (British Cardiac Society). 2006;92(12):1838–43. https://doi.org/10.1136/hrt.2006.093849.
22. Nanna M, Stergiopoulos K. Pregnancy complicated by valvular heart disease: an update. J Am Heart Assoc. 2014;3(3):e000712. https://doi.org/10.1161/jaha.113.000712.
23. Shotan A, Widerhorn J, Hurst A, Elkayam U. Risks of angiotensin-converting enzyme inhibition during pregnancy: experimental and clinical evidence, potential mechanisms, and recommendations for use. Am J Med. 1994;96(5):451–6.
24. Torfgard KE, Ahlner J. Mechanisms of action of nitrates. Cardiovasc Drugs Ther. 1994;8(5):701–17.
25. McComb MN, Chao JY, Ng TM. Direct vasodilators and sympatholytic agents. J Cardiovasc Pharmacol Ther. 2016;21(1):3–19. https://doi.org/10.1177/1074248415587969.
26. Thadani U, Jacob RG. Isosorbide dinitrate/hydralazine: its role in the treatment of heart failure. Drugs Today (Barcelona, Spain: 1998). 2008;44(12):925–37. https://doi.org/10.1358/dot.2008.44.12.1131826.
27. Ladner HE, Danielsen B, Gilbert WM. Acute myocardial infarction in pregnancy and the puerperium: a population-based study. Obstet Gynecol. 2005;105(3):480–4. https://doi.org/10.1097/01.aog.0000151998.50852.31.
28. James AH, Jamison MG, Biswas MS, Brancazio LR, Swamy GK, Myers ER. Acute myocardial infarction in pregnancy: a United States population-based study. Circulation. 2006;113(12):1564–71. https://doi.org/10.1161/circulationaha.105.576751.
29. Elkayam U, Jalnapurkar S, Barakkat MN, Khatri N, Kealey AJ, Mehra A, et al. Pregnancy-associated acute myocardial infarction: a review of contemporary experience in 150 cases between 2006 and 2011. Circulation. 2014;129(16):1695–702. https://doi.org/10.1161/circulationaha.113.002054.
30. Roth A, Elkayam U. Acute myocardial infarction associated with pregnancy. J Am Coll Cardiol. 2008;52(3):171–80. https://doi.org/10.1016/j.jacc.2008.03.049.
31. Manalo-Estrella P, Barker AE. Histopathologic findings in human aortic media associated with pregnancy. Arch Pathol. 1967;83(4):336–41.
32. Havakuk O, Goland S, Mehra A, Elkayam U. Pregnancy and the risk of spontaneous coronary artery dissection: an analysis of 120 contemporary cases. Circ Cardiovasc Interv. 2017;10(3):e004941. https://doi.org/10.1161/circinterventions.117.004941.
33. Demakis JG, Rahimtoola SH. Peripartum cardiomyopathy. Circulation. 1971;44(5):964–8.
34. Tidswell M. Peripartum cardiomyopathy. Crit Care Clin. 2004;20(4):777–88.

xi. https://doi.org/10.1016/j.ccc.2004.05.007.

35. Carro-Jimenez EJ, Lopez JE. Primary pulmonary hypertension and pregnancy. Bol Asoc Med PR. 2005;97(4):328–33.
36. Pieper PG, Hoendermis ES. Pregnancy in women with pulmonary hypertension. Neth Heart J. 2011;19(12):504–8. https://doi.org/10.1007/s12471-011-0219-9.

37. Hemnes AR, Kiely DG, Cockrill BA, Safdar Z, Wilson VJ, Al Hazmi M, et al. Statement on pregnancy in pulmonary hypertension from the Pulmonary Vascular Research Institute. Pulmonary Circulation. 2015;5(3):435–65. https://doi.org/10.1086/682230.
38. Thomas E, Yang J, Xu J, Lima FV, Stergiopoulos K. Pulmonary hypertension and pregnancy outcomes: insights from the national inpatient sample. J Am Heart Assoc. 2017;6(10):e006144. https://doi.org/10.1161/JAHA.117.006144.
39. Hibbard JU, Lindheimer M, Lang RM. A modified definition for peripartum cardiomyopathy and prognosis based on echocardiography. Obstet Gynecol. 1999;94(2):311–6.
40. Ansari AA, Fett JD, Carraway RE, Mayne AE, Onlamoon N, Sundstrom JB. Autoimmune mechanisms as the basis for human peripartum cardiomyopathy. Clin Rev Allergy Immunol. 2002;23(3):301–24. https://doi.org/10.1385/criai:23:3:301.
41. Sundstrom JB, Fett JD, Carraway RD, Ansari AA. Is peripartum cardiomyopathy an organ-specific autoimmune disease? Autoimmun Rev. 2002;1(1–2):73–7.
42. Melvin KR, Richardson PJ, Olsen EG, Daly K, Jackson G. Peripartum cardiomyopathy due to myocarditis. N Engl J Med. 1982;307(12):731–4. https://doi.org/10.1056/nejm198209163071207.
43. Geva T, Mauer MB, Striker L, Kirshon B, Pivarnik JM. Effects of physiologic load of pregnancy on left ventricular contractility and remodeling. Am Heart J. 1997;133(1):53–9.
44. Lampert MB, Hibbard J, Weinert L, Briller J, Lindheimer M, Lang RM. Peripartum heart failure associated with prolonged tocolytic therapy. Am J Obstet Gynecol. 1993;168(2):493–5.
45. Mann DL. Stress-activated cytokines and the heart: from adaptation to maladaptation. Annu Rev Physiol. 2003;65:81–101. https://doi.org/10.1146/annurev.physiol.65.092101.142249.
46. Pierce JA, Price BO, Joyce JW. Familial occurrence of postpartal heart failure. Arch Intern Med. 1963;111:651–5.
47. Novak Z, Thurmond AS, Ross PL, Jones MK, Thornburg KL, Katzberg RW. Gadolinium-DTPA transplacental transfer and distribution in fetal tissue in rabbits. Investig Radiol. 1993;28(9):828–30.
48. Elkayam U, Tummala PP, Rao K, Akhter MW, Karaalp IS, Wani OR, et al. Maternal and fetal outcomes of subsequent pregnancies in women with peripartum cardiomyopathy. N Engl J Med. 2001;344(21):1567–71. https://doi.org/10.1056/nejm200105243442101.
49. Cooper WO, Hernandez-Diaz S, Arbogast PG, Dudley JA, Dyer S, Gideon PS, et al. Major congenital malformations after first-trimester exposure to ACE inhibitors. N Engl J Med. 2006;354(23):2443–51. https://doi.org/10.1056/NEJMoa055202.
50. Pucci M, Sarween N, Knox E, Lipkin G, Martin U. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers in women of childbearing age: risks versus benefits. Expert Rev Clin Pharmacol. 2015;8(2):221–31. https://doi.org/10.1586/17512433.2015.1005074.
51. Hilfiker-Kleiner D, Kaminski K, Podewski E, Bonda T, Schaefer A, Sliwa K, et al. A cathepsin D-cleaved 16 kDa form of prolactin mediates postpartum cardiomyopathy. Cell. 2007;128(3):589–600. https://doi.org/10.1016/j.cell.2006.12.036.
52. Haghikia A, Podewski E, Berliner D, Sonnenschein K, Fischer D, Angermann CE, et al. Rationale and design of a randomized, controlled multicentre clinical trial to evaluate the effect of bromocriptine on left ventricular function in women with peripartum cardiomyopathy. Clin Res Cardiol. 2015;104(11):911–7. https://doi.org/10.1007/s00392-015-0869-5.
53.•• Arrigo M, Blet A, Mebazaa A. Bromocriptine for the treatment of peripartum cardiomyopathy: welcome on BOARD. Eur Heart J. 2017;38(35):2680–2. https://doi.org/10.1093/eurheartj/ehx428.

Bromocriptine is a therapeutic intervention for PPCM that acts as a prolactin antagonist.

54. Arany Z, Elkayam U. Peripartum cardiomyopathy. Circulation. 2016;133(14):1397–409. https://doi.org/10.1161/circulationaha.115.020491.
55. Dunkman WB, Johnson GR, Carson PE, Bhat G, Farrell L, Cohn JN. Incidence of thromboembolic events in congestive heart failure. The V-HeFT VA cooperative studies group. Circulation. 1993;87(6 Suppl):Vi94–101.
56.•• Biteker M, Kayatas K, Duman D, Turkmen M, Bozkurt B. Peripartum cardiomyopathy: current state of knowledge, new developments and future directions. Curr Cardiol Rev. 2014;10(4):317–26.

PPCM with EF < 30–35% warrants anticoagulation.

57. Sliwa K, Hilfiker-Kleiner D, Petrie MC, Mebazaa A, Pieske B, Buchmann E, et al. Current state of knowledge on aetiology, diagnosis, management, and therapy of peripartum cardiomyopathy: a position statement from the Heart Failure Association of the European Society of Cardiology Working Group on peripartum cardiomyopathy. Eur J Heart Fail. 2010;12(8):767–78. https://doi.org/10.1093/eurjhf/hfq120.
58. Lata I, Gupta R, Sahu S, Singh H. Emergency management of decompensated peripartum cardiomyopathy. J Emerg Trauma Shock. 2009;2(2):124–8. https://doi.org/10.4103/0974-2700.50748.
59. Horlocker TT, Wedel DJ, Rowlingson JC, Enneking FK, Kopp SL, Benzon HT, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (third edition). Reg Anesth Pain Med. 2010;35(1):64–101.
60. Leffert L, Butwick A, Carvalho B, Arendt K, Bates SM, Friedman A, et al. The Society for Obstetric Anesthesia and Perinatology consensus statement on the anesthetic management of pregnant and postpartum women receiving thromboprophylaxis or higher dose anticoagulants. Anesth Analg.

2018;126(3):928–44. https://doi.org/10.1213/ane.0000000000002530.
61. Rigatelli G, Rigatelli G. Congenital heart diseases in aged patients: clinical features, diagnosis, and therapeutic indications based on the analysis of a twenty five-year Medline search. Cardiol Rev. 2005;13(6):293–6.
62. Bassily-Marcus AM, Yuan C, Oropello J, Manasia A, Kohli-Seth R, Benjamin E. Pulmonary hypertension in pregnancy: critical care management. Pulm Med. 2012;2012:709407. https://doi.org/10.1155/2012/709407.
63. Dimopoulos K, Inuzuka R, Goletto S, Giannakoulas G, Swan L, Wort SJ, et al. Improved survival among patients with Eisenmenger syndrome receiving advanced therapy for pulmonary arterial hypertension. Circulation. 2010;121(1):20–5. https://doi.org/10.1161/circulationaha.109.883876.
64. Chau EM, Fan KY, Chow WH. Effects of chronic sildenafil in patients with Eisenmenger syndrome versus idiopathic pulmonary arterial hypertension. Int J Cardiol. 2007;120(3):301–5. https://doi.org/10.1016/j.ijcard.2006.10.018.
65.•• Dunn L, Flenady V, Kumar S. Reducing the risk of fetal distress with sildenafil study (RIDSTRESS): a double-blind randomised control trial. J Transl Med. 2016;14(15):15. https://doi.org/10.1186/s12967-016-0769-0.
Sildenafil can be used to treat pulmonary hypertension in the parturient and may also increase uterine blood flow.
66. Cosa N, Costa E Jr. Inhaled pulmonary vasodilators for persistent pulmonary hypertension of the newborn: safety issues relating to drug administration and delivery devices. Medical devices (Auckland, NZ). 2016;9:45–51. https://doi.org/10.2147/mder.s99601.
67. Hankins GD, Berryman GK, Scott RT Jr, Hood D. Maternal arterial desaturation with 15-methyl prostaglandin F2 alpha for uterine atony. Obstet Gynecol. 1988;72(3 Pt 1):367–70.