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REVIEW ARTICLE

Obstetric anesthesia management of the patient with cardiac disease

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ABSTRACT
Cardiovascular disease is the leading cause of maternal mortality in much of the developed world. Risk stratification models can predict which patients are at greatest risk for maternal or fetal morbidity or mortality. Particular cardiac diseases hold significant risk of mortality during pregnancy including pulmonary hypertension, aortic aneurysm, left-ventricular outflow tract obstruction, and severe cardiomyopathy. High-risk patients should deliver at high-resource hospitals under the care of experts in cardiology, obstetrics, perinatology, neonatology and anesthesiology. The obstetric anesthesiologist should formulate delivery plans for cardiac monitoring, labor analgesia, cesarean anesthesia, postpartum monitoring, as well as plans for obstetric or cardiac emergencies. Carefully co-ordinated multidisciplinary care of pregnant women with cardiac disease can result in successful outcomes.

Keywords: Cardiac disease; Pregnancy; Obstetric anesthesia; Obstetric analgesia; Cesarean delivery

Introduction

The number of pregnant women with cardiovascular disease is steadily growing because of improved survival among children born with congenital heart disease (CHD), as well as the increasing frequency of cardiovascular risk factors among women of childbearing age.[1–2] At present, cardiovascular disease is the leading cause of maternal mortality in much of the developed world.[3–5] To reverse this trend, a multidisciplinary team of cardiologists, obstetricians, perinatologists, neonatologists and anesthesiologists must work together to manage these complex patients.[1,6–8]

Risk stratification

Cardiovascular risk during pregnancy and the postpartum period is heterogeneous, depending on the underlying anatomy and physiology. While some patients with simple defects such as restrictive ventricular septal defect, closed patent ductus arteriosus, or mild pulmonary stenosis have no detectable risk above the general population, other conditions pose a serious threat to life in the setting of pregnancy.[9] Thus, patients with pre-existing cardiac conditions should undergo risk stratification, preferably pre-conceptually, to allow for adequate counseling and delivery planning.[1,6,10]

Since high-risk patients may require significant expertise, clinicians can use risk stratification models to justify the transfer of high-risk parturients from low-resource to high-resource hospitals. Several risk stratification models are currently available (Tables 1–4). The CARPREG I, CARPREG II and ZAHARA risk scores identify individual maternal risk factors that are used to calculate a risk score.[11–13] The risk score correlates with an estimated likelihood of a major adverse cardiovascular event. The World Health Organization (WHO) risk stratification model uses cumulative knowledge of lesion-specific risk to divide patients into four risk groups:[9]

- I – risk no greater than general population
- II – small increased risk of maternal death/complications
- III – significant risk of maternal death/complications; requires expert cardiovascular and obstetric care
- IV – pregnancy contraindicated due to very high risk of maternal death or complications

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Table 1 CARPREG I risk score

Risk factors	Points
Prior cardiac event or arrhythmia	1
NYHA class >II or cyanosis	1
Left heart obstruction	1
Systemic ventricular dysfunction (EF <40%)	1
Total score	**Risk of cardiac complications**
0 points	5%
1 point	27%
>2 points	75%

NYHA: New York Heart Association; EF: ejection fraction; From: Siu SC, Sermer M, Colman JM, et al. Prospective multicenter study of pregnancy outcomes in women with heart disease. *Circulation* 2001; **104**: 515–21.

Table 2 CARPREG II risk score

Risk factors	Points
Prior cardiac event or arrhythmia	3
NYHA class >II or cyanosis	3
Mechanical valve	3
Ventricular dysfunction	2
High-risk left-sided valve disease/ LVOT obstruction	2
Pulmonary hypertension	2
Coronary artery disease	2
High-risk aortopathy	2
No prior cardiac intervention	1
Late pregnancy assessment	1
Total score	**Risk of cardiac complications**
0–1 points	5%
2 point	10%
3 points	15%
4 points	22%
>4 points	41%

NYHA: New York Heart Association; LVOT: left ventricular outflow tract; From: Silverside CK, Grewal JM, Mason J, et al. Pregnancy outcomes in women with heart disease: the CARPREG II study. *J Am Coll Cardiol* 2018;**71**:2419–30.

Table 3 ZAHARA risk score

Risk factors	Points
Mechanical valve prosthesis	4.25
Left heart obstruction	2.5
History of arrhythmia	1.5
Cardiac medication prior to pregnancy	1.5
Cyanotic heart disease (corrected or uncorrected)	1.0
NYHA class $\geq$ II	0.75
Systemic atrioventricular valve regurgitation >mild	0.75
Pulmonic atrioventricular valve regurgitation >mild	0.75
Total score	**Risk of cardiac complications**
0–0.5 points	2.9%
0.51–1.5 points	7.5%
1.51–2.5 points	17.5%
2.51–3.5 points	43.1%
>3.51 points	70%

NYHA: New York Heart Association; From: Drenthen W, Boersma E, Balci A, et al. Predictors of pregnancy complications in women with congenital heart disease. *Eur Heart J* 2010; **31**: 2124–32.

Table 4 WHO classification for pregnancy

Risk classification	Cardiac lesions
I – No detectable increased risk of maternal mortality and no or minimal increase in maternal morbidity	- Uncomplicated mild pulmonary stenosis - Ventricular septal defect - Patent ductus arteriosus - Mitral valve prolapse with no more than trivial mitral regurgitation - Successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, anomalous pulmonary venous drainage) - Isolated ventricular extrasystoles and atrial ectopic beats
II – Small increased risk of maternal mortality or moderate increase in morbidity	- Unoperated atrial or ventricular septal defect - Repaired tetralogy of Fallot - Most arrhythmias
II–III – Depending on patient	- Hypertrophic cardiomyopathy - Native or tissue valvular heart disease not considered WHO I or IV - Repaired coarctation - Marfan syndrome without aortic dilatation - Bicuspid valve with aorta <45 mm - Mild ventricular impairment - Heart transplantation
III – Significantly increased risk of maternal mortality or severe morbidity, and expert cardiac and obstetric pre-pregnancy, antenatal, and postnatal care are required	- Mechanical valve - Systemic RV - Fontan circulation - Unrepaired cyanotic heart disease - Other complex congenital heart disease - Marfan syndrome with aorta 40–45 mm - Bicuspid aortic valve with aorta 45–50 mm
IV – Pregnancy is contraindicated	- Pulmonary hypertension - Eisenmenger syndrome - Systemic ventricular EF <30% - Systemic ventricular dysfunction with NYHA class III–IV - Severe mitral stenosis - Severe symptomatic aortic stenosis - Marfan syndrome with aorta >45 mm - Bicuspid aortic valve with aorta >50 mm - Native severe coarctation - Prior peripartum cardiomyopathy with any residual impairment of ventricular function

WHO: World Health Organization; EF: ejection fraction; NYHA: New York Heart Association; RV: right ventricle; From: Thorne S, MacGregor A, Nelson-Piercy C. Risks of contraception and pregnancy in heart disease.

In a validation study of CARPREG I, ZAHARA and the WHO risk stratification model it was identified that while none of these models is ideal, the WHO classification model performed the best at predicting maternal complications.[14] The CARPREG II was not included because it was only recently published and has not yet undergone comparison to the other models.[13]

Fortunately, with expert multidisciplinary care, most women with cardiovascular disease can experience a safe pregnancy and delivery. However, certain cardiovascular conditions are associated with a high risk of maternal morbidity and mortality, and pregnancy should be discouraged in women with these conditions.[1,9] In these patients, if pregnancy is achieved and termination is declined, they should be managed as WHO class III patients with expert multidisciplinary care in the highest-resource hospital possible with careful monitoring for clinical decompensation during and in the first 72 hours after delivery.

High risk cardiac conditions

Pulmonary arterial hypertension (PAH) is associated with a 30–56% risk of maternal mortality.[15] The risk is greater in patients with more severely elevated pulmonary arterial pressures and pulmonary vascular resistance, worse functional class, and pre-existing right ventricular dysfunction. Pulmonary vasodilators including phosphodiesterase (PDE-5) inhibitors, prostacyclins, calcium channel blockers, and nitric oxide should be continued during pregnancy or promptly initiated in appropriate patients if the diagnosis is made during pregnancy.[16–18] Endothelin receptor antagonists (e.g. ambrisentan, bosentan or macitentan) are teratogenic and should be discontinued upon discovery of pregnancy.[16,17]

Pregnancy is also associated with excessive maternal morbidity and mortality in women with aortic aneurysms, particularly when associated with heritable aortopathies such as Marfan Syndrome, Loeys-Dietz Syndrome, or Ehlers-Danlos Syndrome.[19,20] There is

about a 10% risk of aortic dissection during pregnancy or the peripartum period in patients with a maximal aortic diameter exceeding 40 mm, rapid dilation, or prior dissection, in patients with Marfan Syndrome.[21] Patients with Ehlers-Danlos Type IV are at risk for dissection even in the absence of dilatation.[1] Patients with bicuspid aortic valve associated aortopathy seem to be at lower risk of aortic dissection, and pregnancy is considered reasonable up to an aortic diameter of 50 mm.[1] Beta-blockers are recommended during pregnancy and the peripartum period in women with aortopathy, to reduce the risk of dissection.[1]

Left-sided obstructive heart disease, including coarctation of the aorta and aortic and mitral valve stenosis, is associated with significant maternal morbidity when severe and symptomatic.[1] As cardiac output increases throughout pregnancy and during delivery, the pressure gradient across the fixed stenotic lesion will increase.[21,22] This predisposes the patient to pulmonary vascular congestion, pulmonary hypertension, and atrial arrhythmias.[1] Such patients are also at risk for myocardial ischemia in the setting of acute decreases in systemic vascular resistance. Patients with severe symptoms refractory to medical management may be considered for balloon valvuloplasty during pregnancy, if their anatomy is favorable.[1]

Pregnancy carries an excessive maternal risk in patients with severe cardiomyopathy (systemic ventricular ejection fraction <30% or New York Heart Association Class III–IV) or those diagnosed with peripartum cardiomyopathy in a prior pregnancy with residual left ventricular dysfunction (ejection fraction <50%).[9] Women with dilated cardiomyopathy are at increased risk of symptomatic heart failure during the third trimester and postpartum periods.[23] Patients with a history of peripartum cardiomyopathy and residual left ventricular dysfunction carry about a 50% risk of recurrent heart failure symptoms and about a 25% risk of mortality.[24–26] Angiotensin converting-enzyme inhibitors, angiotensin receptor blockers, and aldosterone antagonists are potentially teratogenic and should be discontinued on discovery of pregnancy.[23,27] Afterload reduction can be achieved with hydralazine during pregnancy.[23] Beta-blockers including carvedilol and metoprolol are generally safe during pregnancy and should be continued in women with pre-existing cardiomyopathy.[23,27]

Delivery planning

Multidisciplinary delivery planning is necessary for patients at high risk of cardiovascular complications.[1,6] Coordinated care requires input from anesthesiologists, obstetricians, cardiologists, and neonatologists with experience in the management of these complex patients.[6] The predicted effects of pregnancy on various cardiac lesions and the resultant anesthetic goals are reviewed in Table 5. Regarding obstetric management, for the majority of cardiac patients, vaginal delivery remains the safest option, barring obstetric indications for cesarean delivery.[1,6,28] Vaginal delivery is associated with less blood loss, reduced infection rates, and reduced thrombosis risk.[1,28] However, planned cesarean delivery may be preferred in the highest risk patients, as it avoids the need for emergent delivery and permits the attendance of all relevant consultants.

Cesarean delivery is typically recommended in patients with Marfan or Loeys-Dietz syndrome with an aortic diameter >4.5 cm, bicuspid aortopathy with aortic diameter >5.0 cm, and all patients with Ehlers-Danlos Type IV regardless of aortic diameter. Likely, labor will not be well tolerated by women with intractable heart failure symptoms, and cesarean delivery should be considered.[1] Other high-risk conditions including severe pulmonary hypertension and severe left-sided obstructive lesions may also be considered for cesarean delivery.[1] Patients who have recently taken oral vitamin K antagonists should also undergo cesarean delivery to reduce the risk of fetal hemorrhagic complications.[1]

An alternative delivery approach to spontaneous vaginal delivery is sometimes termed a "cardiac vaginal delivery."[29,30] In this type of delivery, when complete cervical dilation is achieved, the parturient does not push. Instead, the uterus continues to contract as it did during the first stage of labor, and the uterus "labors down" the fetus. When the fetal head becomes low enough, the obstetrician performs a low-outlet forceps or vacuum-assisted delivery.[6,28] There is debate whether a cardiac vaginal delivery is appropriate among parturients with heart disease.[29] While some believe avoidance of Valsalva maneuvers is hemodynamically favorable for some patients, others feel that the prolongation of the passive (non-pushing) second stage as well as the instrumented delivery can lead to obstetric and neonatal complications.[30] Of note, prolonged and intense Valsalva maneuvers may be poorly tolerated in women with certain cardiac conditions due to the reduction in preload and increase in afterload that occurs during the Valsalva and the overshoot in cardiac output that occurs upon release.[31,32] In particular, women with pulmonary hypertension, fixed stenotic lesions, ventricular dysfunction, single ventricles, and moderate degrees of aortic dilation may be candidates for a cardiac vaginal delivery.[6]

Cardiac monitoring

Appropriate cardiac monitoring during labor can predict and prevent maternal cardiac or obstetric events. Pulse oximetry with a visible photoelectric plethysmographic waveform during labor allows care providers to determine the accuracy of the pulse oximetry reading. Therefore, cardiac parturients may require two pulse oximeters—one that is attached to the tocodynamome-

Table 5 Pregnancy effects and anesthetic goals for cardiovascular disease in pregnancy

	Physiologic Effects of Pregnancy and Delivery	Anesthetic Goals
Coronary Artery Disease	(-) The decreased SVR of pregnancy can result in lesser coronary perfusion to the myocardium. (-) The increase in HR during pregnancy can result in decreased coronary filling time (-) Cardiac work can increase significantly during labor, especially painful labor	Normal heart rate (avoid tachycardia) → *Excellent labor analgesia* → *Continue beta blockade through labor and delivery* → *Avoid beta agonist agents (e.g. terbutaline)* Maintain afterload → *Consider intra-arterial blood pressure monitoring* → *Phenylephrine is vasopressor of choice* → *Careful titration of onset of neuraxial anesthetic for labor or CD* → *Consider phenylephrine infusion for CD* → *Titrate oxytocin carefully* Monitor for and avoid ischemia → *5-lead ECG monitoring for CD or labor* → *Avoid methylergonovine* Postpartum monitoring → *Monitor for postpartum ischemia or heart failure*
Severe LV Dysfunction (e.g. dilated or peripartum cardiomyopathy)	(-) The increase in cardiac output and blood volume during pregnancy can result in heart failure/pulmonary edema (-) The decrease in oncotic pressure during pregnancy can result in greater risk for pulmonary edema (-) Angiotensive converting enzyme inhibitors must be stopped during pregnancy secondary to teratogenicity (-) Patients with a prior episode of peripartum cardiomyopathy are at risk for further deterioration in LV function with subsequent pregnancies	Normal heart rate (avoid bradycardia) → *Treat bradycardia with ephedrine or glycopyrrolate* Maintain afterload (avoid hypertension or hypotension) → *Consider intra-arterial blood pressure monitoring* → *Excellent labor analgesia* → *Careful titration of onset of regional anesthetic for labor or CD* → *Treat hypotension with ephedrine or norepinephrine as needed.* → *Titrate oxytocin carefully* Maintain contractility → *Ephedrine is vasopressor of choice* → *If low cardiac output syndrome develops consider milrinone or dobutamine with the addition of epinephrine or norepinephrine to maintain blood pressure* Maintain normovolemia → *Strict monitoring of fluid balance* Prevent/ Monitor for pulmonary edema → *Careful fluid balance* → *Continuous pulse oximetry throughout labor and peripartum (including postpartum)* Manage pulmonary edema → *Consider diuresis* → *Administer supplemental oxygen* → *If necessary, consider intubation with PEEP and controlled ventilation* Manage AICD if present → *Keep anti-tachyarrhythmia function of AICD active in labor* → *Assure preparations to suspend this function in the event of emergent CD* Minimize pulmonary vascular resistance → *Administer supplemental oxygen throughout labor and delivery* → *Avoid over-sedation* → *Assure well-controlled ventilation if intubated* → *Avoid carboprost* Postpartum monitoring → *Monitor for postpartum heart failure*

(*continued on next page*)

ter machine to detect concurrence of the measured fetal and maternal heart rate, as well as one attached to a separate maternal monitor which displays the pulse oximetry wave form. Closely monitored pulse oximetry is important for all cardiac patients, but especially for any patient with a shunt lesion. Drops in systemic vascular resistance in patients with a shunt may be accompanied by a decrease in oxygenation. The pulse oximetry waveform allows the provider to more quickly determine if unusual electrical activity displayed on the 5-lead electrocardiographic telemetry is artifact or pulseless arrhythmic event. In the former, the waveform will continue to display normally, in the latter the waveform will be absent indicating no pulse.

Maternal 5-lead electrocardiographic (ECG) telemetry should be considered for any patient who is at risk for arrhythmia or ischemia during labor. Non-invasive blood pressure (NIBP) monitoring should be performed at regular intervals, and consideration given to arterial line placement for parturients at high risk of decompen-

Table 5 (*continued*)

Pulmonary Hypertension	(-) The increased cardiac output of pregnancy may not be accommodated by the fixed pulmonary vasculature resulting in right heart failure and death (-) The decreased SVR of pregnancy can decrease coronary filling to a dilating and failing right ventricle (-) The hypercoagulable state of pregnancy can result in pulmonary emboli which are especially lethal in patients with pulmonary hypertension	Minimize pulmonary vascular resistance → *Administer supplemental oxygen throughout labor and delivery* → *Avoid over-sedation* → *Assure well-controlled ventilation if intubated* → *Avoid carboprost* Maintain adequate blood volume and venous return → *Strict monitoring of fluid balance* Avoid myocardial depressants → *Avoid beta blockade if possible* → *5-lead ECG monitoring for CD or labor* Maintain afterload → *Consider intra-arterial blood pressure monitoring* → *Careful titration of onset of neuraxial anesthetic for labor or CD* → *Phenylephrine is vasopressor of choice* → *Titrate oxytocin carefully* Invasive pulmonary artery catheter monitoring as well as vasoactive agents may be necessary → *Consider partnership with cardiovascular anesthesiologist* Postpartum monitoring → *Monitor for postpartum right heart failure*
Unstable Arrhythmia History	(-) Pregnancy, labor and delivery can trigger tachyarrhythmias	Identify arrhythmias early → *5-lead ECG monitoring during CD or vaginal delivery and postpartum* → *Nursing staff must be qualified to monitor cardiac telemetry* Cardiovert unstable arrhythmias rapidly → *Cardioversion can be performed in pregnancy* → *In tachyarrhythmia, consider fetal distress indication for cardioversion* Manage pacemaker/AICD if present → *Keep anti-tachyarrhythmia function of AICD active in labor* → *Assure preparations to suspend AICD function and initiate VOO mode in the event of emergent CD* Postpartum monitoring → *Monitor for postpartum arrhythmia*
Aortopathy (e.g. Marfan syndrome)	(-) Pregnancy, labor and delivery may increase dilation of aortic root (-) Pregnancy, labor and delivery increases the risk of aortic rupture in women with Marfan syndrome	Minimize aortic wall tension → *Excellent labor analgesia* → *Continue beta blockade through labor and delivery* → *CD or no Valsalva during second stage labor may be recommended by OB/CV* Minimize hemodynamic swings → *Careful titration of onset of neuraxial anesthetic for labor or CD* → *Consider intra-arterial blood pressure monitoring* → *Avoid methylergonovine and carboprost* → *Titrate oxytocin carefully* Postpartum monitoring → *Monitor for postpartum hemodynamic instability*
Valvular Lesions		
Mechanical Prosthetic Valve	(-) Hypercoagulable state of pregnancy increases risk of valve thrombosis (-) Vitamin K antagonists (most effective way to prevent valvular clot formation) are teratogenic often resulting in suboptimal anticoagulation regimens during pregnancy	Balance risk of anticoagulation therapy and anesthesia technique → *Perform general anesthesia for CD in patients who are anticoagulated* Recognize anticoagulation also increases risk of intrapartum and postpartum hemorrhage → *Select and/or titrate uterotonics carefully depending on underlying cardiac disease recognizing that oxytocin decreases SVR, methylergonovine behaves as an adrenergic alpha agonist and carboprost increases pulmonary vascular resistance significantly* Postpartum monitoring → *Monitor for postpartum valvular clotting or obstetric bleeding*

(*continued on next page*)

sating with hypo- or hypertension. The arterial line can facilitate blood pressure management during an unexpected cardiac or obstetric event. For example, if the need arises to induce general anesthesia rapidly for fetal or maternal distress, the anesthesia team can use the arterial line to determine the beat-to-beat blood pressure and thereby titrate a rapid induction to allow for hemodynamic stability. Likewise, if an epidural needs to be rapidly dosed for cesarean delivery, the anesthesia team can titrate a vasopressor to beat-to-beat blood pressure

Table 5 (*continued*)

Mitral Stenosis	(-) Because of relatively fixed preload to the LV, the heart may not be able to generate increased cardiac output and pulmonary edema will develop (-) Decreased oncotic pressure further increases risk of pulmonary edema (-)The increase in blood volume and heart rate in pregnancy increases left atrial pressure and may lead to atrial fibrillation and pulmonary edema	Normal heart rate (avoid tachycardia) → *Excellent labor analgesia* → *Continue beta blockade through labor and delivery* → *5-lead ECG monitoring for CD or labor* → *Avoid beta agonist agents (e.g. terbutaline)* Avoid Atrial fibrillation → *In new atrial fibrillation, cardioversion should be considered* → *In failed cardioversion and in cases with chronic atrial fibrillation, decrease rapid ventricular rate with medical treatment* Maintain normovolemia → *Strict monitoring of fluid balance* Prevent/ Monitor for pulmonary edema → *Careful fluid balance* → *Continuous pulse oximetry throughout labor and peripartum (including postpartum)* Manage pulmonary edema → *Consider diuresis* → *Administer supplemental oxygen* → *If necessary, consider intubation with PEEP and controlled ventilation* Postpartum monitoring → *Monitor for postpartum pulmonary edema*
Aortic Stenosis	(-)The decreased SVR of pregnancy can result in lesser coronary perfusion pressure to the thickened LV myocardium (-) Because of LV diastolic dysfunction, excess volume can lead to pulmonary edema	Maintain afterload (avoid hypotension) → *Consider intra-arterial blood pressure monitoring* → *Careful titration of onset of neuraxial anesthetic for labor or CD* → *Treat hypotension with phenylephrine* → *Avoid beta agonist agents (e.g. terbutaline)* → *Titrate oxytocin carefully* Normal heart rate (avoid tachycardia) → *Excellent labor analgesia* Monitor for ischemia → *5-lead ECG monitoring for CD or labor* Maintain normovolemia → *Strict monitoring of fluid balance* Postpartum monitoring → *Monitor for postpartum hypotension or ischemia*
Mitral / Aortic Insufficiency	(+)The decreased SVR results in a lesser regurgitant volume (-) Pregnancy can worsen ventricular dilation	Avoid increases in SVR and decreases in contractility → *Excellent labor analgesia* Avoid bradycardia → *Careful titration of vasopressors (e.g. phenylephrine) with spinal for CD* Maintain sinus rhythm → *Excellent labor analgesia* Consider afterload reduction → *Neuraxial analgesia/anesthesia typically well tolerated if preserved ventricular function*

(*continued on next page*)

measurements. Further, intra-arterial blood pressure monitoring along with a pulse oximeter waveform can be used to determine if any arrhythmic events compromise perfusion.

Because laboring women often move, breathe spontaneously and sometimes push, the measurement of a central venous pressure (CVP) is difficult to interpret. Likewise, in laboring women, pulmonary arterial catheter (PAC) monitoring is typically not useful. Notably, there are unique circumstances for which CVP or PAC monitoring is indicated, such as a laboring patient with severe pulmonary hypertension who requires a continuous infusion of pulmonary vasodilatory medications.

Most cardiac parturients should have baseline transthoracic echocardiography (TTE) performed prior to presenting to labor and delivery. Clinical changes from baseline during labor, such as a decrease in oxygenation or blood pressure, can be evaluated with TTE monitoring. Of note, obtaining TTE images in labor may be difficult or impossible secondary to lack of equipment, lack of TTE training amongst staff, lack of patient co-operation in labor, or lack of time in the case of an emergency. In the event a patient is under general anesthesia, transesophageal echocardiography (TEE) is an option. In the future, non-invasive cardiac output monitoring via arterial waveform monitoring techniques such as PiCCO™, LiDCO™, or FloTrac™ may prove clinically useful in the laboring cardiac parturient. At this time, for most cardiac parturients in labor, pulse oximetry with a visible plethysmographic

Table 5 (*continued*)

Shunt Lesions		
R to L Shunt (e.g. TOF, Eisenmenger's)	(-)The decrease in SVR increases right-to-left shunting and possible cyanosis (+)In unrepaired TOF and normal RV function, the increase in blood volume is beneficial because adequate RV preload is necessary to eject blood past the outflow obstruction and increase pulmonary blood flow *CCHD, Eisenmenger's and all pulmonary vascular hypertensive diseases, carry a high mortality rate in pregnancy, labor, delivery and the postpartum. Full pregnancy implications and anesthetic management is beyond this table	Avoid decreases in afterload, which can lead to episodes of cyanosis → *Continuous pulse oximetry throughout labor and peripartum (including postpartum)* → *Treat cyanotic episodes with phenylephrine* → *Consider intra-arterial blood pressure monitoring* → *Careful titration of onset of neuraxial anesthetic for labor or CD* → *Titrate oxytocin carefully* Minimize pulmonary vascular resistance → *Administer supplemental oxygen throughout labor and delivery* → *Avoid over-sedation* → *Assure well-controlled ventilation if intubated* → *Avoid carboprost* Maintain adequate blood volume and venous return → *Strict monitoring of fluid balance* → *Avoid supine position* Avoid myocardial depressants, because any decrease in RV contractility can decrease pulmonary circulation → *Avoid beta blockade if possible* → *5-lead ECG monitoring for CD or labor* If pulmonary vascular disease is present, invasive pulmonary artery catheter monitoring as well as vasoactive agents may be necessary → *Consider partnership with cardiovascular anesthesiologist* Avoid paradoxical embolism → *Place filters on intravenous lines* → *Perform epidural loss of resistance technique with saline and not air* Postpartum monitoring → *Monitor for postpartum cyanosis*
L to R Shunt (e.g. VSD **or** ASD)	(+)The decrease in SVR decreases the left-to-right shunting (-)The increase in blood volume can precipitate failure because the patient is in a state of compensatory hypervolemia	Avoid excessive fluid administration, over-transfusion, and Trendelenburg position. → *Strict monitoring of fluid balance* Avoid increases in afterload → *Excellent labor analgesia* Avoid paradoxical embolism → *Place filters on intravenous lines* → *Perform epidural loss of resistance technique with saline and not air*

SVR, systemic vascular resistance; HR, heart rate; CD, cesarean delivery; LV, left ventricle; RV, right ventricle; PEEP, positive end expiratory pressure; AICD, automatic implantable cardioverter defibrillator; CCHD, cyanotic congenital heart disease; ECG, electrocardiogram; VOO, asynchronous ventricular pacing; OB, obstetric; CV, cardiovascular; TOF, tetralogy of Fallot; VSD, ventricular septal defect; ASD, atrial septal defect.

waveform, 5-lead ECG monitoring, and regular NIBP measurements with consideration for intra-arterial blood pressure monitoring is adequate.

Analgesia for vaginal delivery

Effective labor analgesia results in greater cardiopulmonary and hemodynamic stability during labor.[33–35] Painful labor provokes catecholamine release which results in tachycardia, hypertension, hyperventilation, increased cardiac output and increased cardiac oxygen demand.[36] These changes can be detrimental for patients who are at risk for cardiac ischemia, arrhythmias, or rupture of an aneurysm. Therefore, for laboring cardiac patients, most anesthesiologists initiate epidural labor analgesia as early as possible. This may be immediately at the onset of discomfort in spontaneous labor, or at the first sensation of contractions for induced labor.

As previously discussed some obstetricians and cardiologists may recommend a "cardiac vaginal delivery" which involves little to no maternal pushing. As women progress through labor and the cervix dilates, the swings in cardiac output become greater.[37] In order for this type of delivery to successfully limit hemodynamic fluctuations, the labor analgesia technique must provide excellent perineal coverage. Techniques to improve analgesia efficacy and sacral nerve root coverage should be considered. Either epidural-only or combined spinal-epidural (CSE) techniques can be performed. An intrathecal-opioid-only CSE technique may provide a slower onset of sympathectomy and thereby a slower decrease in systemic vascular resistance (SVR). A dural puncture epidural (DPE) technique may provide better quality epidural analgesia with more successful sacral nerve root coverage.[38,39] Whatever the technique, active labor analgesia management with early replacement of ineffective neu-

raxial catheters is important. Further, assuring analgesic efficacy of the epidural catheter during labor may avert the need for a rapid induction of general anesthesia in the event of an emergent cesarean delivery.[40]

Because patients with intra- or extra-cardiac shunts are at risk for paradoxical air embolism, consideration should be given to an epidural loss-of-resistance technique with saline rather than air in the event the epidural needle is inadvertently placed into an epidural vein.[41,42] Further, careful thought should be given to "test dosing" the epidural catheter. If it is thought that the intravenous injection of epinephrine could cause significant harm, then consideration could be given to a local anesthetic-only test dose. Conversely, a catheter inadvertently placed in the intrathecal or intravascular space, not identified, and dosed as an epidural, could be catastrophic for a high-risk cardiac patient.

Anesthesia for cesarean delivery

Neuraxial anesthesia for most patients with cardiac disease undergoing cesarean delivery should be considered.[43] Spinal, epidural, or CSE anesthesia provide the opportunity for the mother to be awake for the birth of her child and for avoidance of the risks of general anesthesia and positive pressure ventilation. The hemodynamic changes associated with neuraxial anesthesia techniques for cesarean delivery are reviewed elsewhere.[44] In brief, the onset of neuraxial anesthesia results in a decrease in venous tone (preload) and a decrease in SVR often resulting in hypotension. Intrathecal local anesthetic provides a more rapid block onset than epidural local anesthetic. Therefore, if a rapid decrease in SVR could cause cardiopulmonary decompensation for a patient, then an epidural would provide a more gradual onset of the hemodynamic changes.

Epidurals, on the other hand, may not provide the density, symmetry or consistency of spinals. Therefore, if an anesthesiologist believes a patient could tolerate a spinal, he or she may proceed with a spinal anesthetic with intra-arterial beat-to-beat blood pressure monitoring and a prophylactic phenylephrine infusion. Some anesthesiologists prefer a sequential CSE technique for cardiac patients, believing that it combines the reliability and symmetry of a spinal with the gradual onset of an epidural anesthetic.[45] In this technique, intrathecal hyperbaric bupivacaine 2.5–5 mg and fentanyl 15–25 μg is followed by 2–3 mL epidural boluses of plain 0.5% bupivacaine or 2% lidocaine over 15 and 30 min after the intrathecal injection. Carefully titrated spinal catheter anesthesia has also been described in cardiac cesarean deliveries.[46]

There are clinical scenarios in which neuraxial anesthesia is not advised. Many cardiac patients are maintained on anticoagulation therapy throughout their pregnancy. Because pregnancy is a pro-coagulant state, patients with a history of deep vein thrombosis, pulmonary emboli, mechanical valves, low ejection fractions, or those who would significantly decompensate from pulmonary emboli (e.g. Fontan circulation) may be anticoagulated with subcutaneous prophylactic or therapeutic unfractionated or low molecular weight heparin.[47] Because mechanical valves in pregnancy carry significant thrombotic and thereby mortality risk,[48] occasionally such patients will be maintained on warfarin anticoagulation in pregnancy.[1] Multiple international and national neuraxial anesthesia associations provide guidance for the performance of neuraxial anesthetic techniques in the presence of anticoagulation therapy.[49–54] A recently published consensus statement on the obstetric anesthetic management of patients receiving anticoagulation therapy discusses this clinical conundrum.[55] In the end, if an anticoagulated patient requires an emergent cesarean delivery and the anticoagulation cannot be reversed, the risk of epidural hematoma from neuraxial anesthesia may outweigh the risks of general anesthesia.

Besides anticoagulation concerns, general anesthesia may be necessary for patients who are unable to lie flat or require mechanical ventilation because of pulmonary edema from heart failure. Further, general anesthesia may be necessary for unstable patients requiring mechanical ventilation for critical illness, for pulmonary vasodilation with inhaled nitric oxide, or for those who are at risk of a hemodynamic disaster such as patients with ongoing myocardial ischemia or a dissecting aorta. In such unstable cases, the obstetric anesthesiology team should consider consulting a cardiac anesthesiology team as early as possible. Alerting the cardiac anesthesia team prior to deterioration can allow this team time to co-ordinate resources such as extracorporeal membrane oxygenation (ECMO) or cardiopulmonary bypass.

Induction of general anesthesia for cesarean delivery in most healthy patients is typically rapid sequence with no premedication. The concerns for administering fentanyl and lidocaine prior to induction include increasing the risks of newborn sedation and maternal aspiration. For the cardiac parturient, many anesthesiologists believe that it is reasonable to prioritize hemodynamic stability over these risks. Therefore, premedication with opioids or lidocaine and a slow titration of induction agents may be reasonable. Some anesthesiologists may choose premedication with remifentanil in the cardiac patient undergoing cesarean delivery because at a dose of 1 μg/kg it has been shown to attenuate the heart rate and blood pressure elevation which can occur with induction, intubation and incision.[56] And, although remifentanil readily crosses the placenta, in comparison to fentanyl it theoretically causes less sedation of the newborn.[56,57] In high-risk cardiac patients undergoing cesarean delivery with an etomidate induction (0.1–0.3 mg/kg), remifentanil can be administered either as a pre-induction infusion at 0.2–0.5μg/kg/min for 5–10 min, or as a single bolus at the time of induction at a dose of 2–4 μg/kg.[58–60]

Whether the patient is undergoing neuraxial or general anesthesia, consideration should be given to the placement of an intra-arterial catheter for blood pressure monitoring. Further, in patients who require general anesthesia secondary to critical illness such as severe pulmonary hypertension, heart failure, myocardial ischemia, or coronary or aortic dissection, central venous access and pulmonary artery catheter placement may be appropriate. Transesophageal echocardiography during cesarean delivery can also be helpful in the unstable patient under general anesthesia.

Postpartum monitoring

The postpartum period is one of the highest risk times for maternal cardiac complications.[17] Immediately following delivery, preload is significantly increased due to relief of inferior vena cava obstruction by the gravid uterus and an "auto-transfusion" of blood from the contracting evacuated uterus.[44,61] This results in an increase in cardiac output through increases in both stroke volume and heart rate.[44] Over the first several days postpartum, extravascular fluid mobilizes into the intravascular compartment, maintaining an elevated preload during this time.[17] Concurrently, cardiac output begins to decrease, while the systemic vascular resistance continues to rise over the first few weeks.[61] In predisposed patients, these hemodynamic changes significantly increase the risk for cardiovascular decompensation.

Many signs and symptoms of heart failure, such as peripheral edema, can be present in normal pregnancy or in the postpartum period.[62] A careful history and physical exam can help distinguish heart failure symptoms from normal pregnancy. Postpartum orthopnea, paroxysmal nocturnal dyspnea and cough should raise suspicion for intravascular volume overload. On examination, jugular venous distension, pulmonary rales, and a prominent third heart sound are consistent with acute heart failure. Pregnant and postpartum women should have an oxygen saturation greater than 95% and any oxygen requirements should be investigated.[63] Clinical biomarkers such as B-type natriuretic peptide (BNP) or NT-proBNP can be useful for differentiating between normal pregnancy physiology and clinical heart failure. The BNP levels are normal in an uncomplicated pregnancy, and BNP $<$100 pg/ml has a 100% negative predictive value for cardiac events in women with pre-existing structural heart disease.[64,65]

Patients who are at risk for decompensation in the postpartum period include those with pulmonary hypertension, right or left heart failure, significant diastolic dysfunction, and left ventricular outflow tract obstruction. In general, patients who are hemodynamically unstable prior to delivery are likely to worsen in the immediate postpartum period and should receive cardiac monitoring in an intensive care environment.

Emergency preparedness

Emergency cesarean delivery in the patient with cardiac disease can pose significant risk to the mother and her fetus. Preparation for emergencies may influence how an anesthesiologist manages a cardiac parturient in labor even if she appears stable. For example, even if a patient with severe aortic stenosis appears to have a stable heart rate and blood pressure in labor, the anesthesiologist may choose to place an intra-arterial catheter for beat-to-beat blood pressure monitoring in the event that a rapid induction of general or neuraxial anesthesia is necessary for emergency cesarean delivery. Likewise, the anesthesiologist may follow a labor epidural more closely and replace a poorly functioning epidural catheter more readily to improve the odds of avoiding general anesthesia for an emergent cesarean delivery.

Emergency cesarean delivery may be a result of fetal distress. Terbutaline and ritodrine are tocolytic agents which may be administered as a component of intrauterine fetal resuscitation.[66,67] Although in the past, these drugs were used as long-term tocolytic agents to prolong pregnancy in preterm labor, they are now more commonly administered intramuscularly or subcutaneously for acute myometrial relaxation in the presence of uterine tachysystole.[66] Terbutaline and ritodrine's $beta_2$ adrenergic effects cause inotropy, chronotropy and significant peripheral vasodilation. Chest pain, EKG ST depression, supraventricular tachycardia, sinus tachycardia and right axis deviation have been described in cardiac pregnant patients who received these medications.[68–69] One could imagine a particularly devastating outcome in a lesion such as hypertrophic obstructive cardiomyopathy—the beta adrenergic effects could cause infundibular spasm and outflow tract obstruction while the peripheral vasodilation decreases coronary perfusion.

A plan for postpartum hemorrhage medical management should be in place for every cardiac parturient. Uterotonic drugs have significant cardiovascular effects. Understanding the cardiovascular effects of these drugs can allow the anesthesiologist to avoid particular agents and counteract the effects of others. Oxytocin should be titrated carefully as it can cause decreases in SVR.[70–72] The decrease in SVR from oxytocin can be counteracted with careful titration of a phenylephrine infusion. Of note, there are reports of oxytocin administration in 5–10 unit bolus doses causing hypotension, tachycardia, ECG ST depression, and even death.[73,74]

Another uterotonic agent, carboprost tromethamine (prostaglandin F2-alpha), can cause significant increase in pulmonary arterial pressures[75,76] and should be avoided in patients with shunt lesions, pulmonary hypertension, right heart dysfunction of any sort, or reactive airway disease. Likewise, methylergonovine is an ergot alkaloid that, along with increasing the contraction strength of myometrial smooth muscle, can

cause vascular smooth muscle contraction resulting in coronary vasospasm, myocardial ischemia,[77] and acute pulmonary hypertension.[78,79] Like carboprost, methylergonovine should be used with extreme caution in most cardiac parturients. Misoprostol is a prostaglandin E1 analogue that is often used for induction of labor. Although it is considered one of the weakest uterotonic agents for the prevention or treatment of postpartum hemorrhage,[80] it has no cardiovascular side effects. Of note, recent studies have not found its prophylactic use effective in preventing postpartum hemorrhage.[81] Therefore, in postpartum hemorrhage, careful titration of an oxytocin infusion as well as rectal or buccal misoprostol are reasonable treatments for the cardiac parturient. In most situations, carboprost and methylergonovine should be avoided.

Women with a history of arrhythmias are at risk for recurrence during pregnancy, labor and delivery.[82] When a pregnant patient has an arrhythmic event, a fetal heart rate monitor should be applied immediately. The fetal status should be considered when deciding whether the arrhythmia is stable. The guidelines for supraventricular tachycardia (SVT) in pregnancy are reviewed elsewhere[83] and are summarized as follows:

- Vagal maneuvers (carotid massage or ice to the face) and adenosine treatment are considered first-line treatment for SVT in pregnancy.
- If these are unsuccessful, stable SVT can be treated with intravenous metoprolol or propranolol.
- If beta blockade is unsuccessful, verapamil and/or procainamide can be used.
- Amiodarone should be considered in pregnancy only if other therapies have failed and if the SVT is life threatening.
- For unstable patients, electrical cardioversion should be performed immediately with the electrode pads positioned normally on the chest being careful to avoid misplacement (i.e. the energy trajectory should not pass through the uterus).
- For bradyarrythmias, temporary external pacing or esophageal pacing is considered safe.
- A fetal scalp electrode lead should be removed prior to electrical cardioversion or pacing.

Guidelines for the management of cardiac arrest in pregnancy are reviewed in depth elsewhere.[84,85] Basic and advanced cardiac life support (ACLS) in pregnancy differ from non-pregnant resuscitation in the following ways:

- Code team members should be familiar with caring for pregnant women and should involve a team dedicated to neonatal resuscitation.
- Pulseless pregnant women should be placed supine with a manual left-uterine-displacement maneuver performed in one of two ways: A two-handed technique with the operator standing on the left side of the patient pulling toward themselves, or a one-handed technique with the operator standing on the right side of the patient pushing away.
- If the uterine fundal height is above the level of the umbilicus, manual uterine displacement should be performed, and a resuscitative hysterotomy (also called perimortem cesarean delivery) should be initiated after four to five minutes from the onset of cardiac arrest at the location that the arrest occurred.[86]
- The recommended ACLS chest compression technique and defibrillation protocol is no different from the non-pregnant guidelines. If a fetal scalp electrode is present, this should be removed prior to defibrillation if possible.
- Intravenous access should be obtained above the diaphragm if possible.
- Epinephrine is preferred over vasopressin. Otherwise, ACLS drugs, including amiodarone, should be administered without modification.

Conclusion

Obstetric anesthesiologists can use validated risk stratification systems and knowledge about high-risk cardiac disease to ensure high-risk pregnant women deliver in high-resource hospitals with expert care. Plans for cardiac monitoring, labor analgesia and cesarean anesthesia should be formulated carefully and the anesthesiologist should be prepared for both obstetric and cardiac emergencies. Coordinated, multidisciplinary care of pregnant women with cardiac disease can result in successful outcomes.

References

1. Regitz-Zagrosek V, Lundqvist CB, Borghi C, et al. ESC Guidelines on the management of cardiovascular diseases during pregnancy; The task force on the management of cardiovascular diseases during pregnancy of the European Society of Cardiology (ESC). *Eur Heart J* 2011;**32**:3147–97.
2. Connolly HM. Pregnancy in women with congenital heart disease. *Curr Cardiol Rep* 2005;**7**:305–9.
3. Creanga AA, Syverson C, Seed K, Callaghan WM. Pregnancy-related mortality in the United States, 2011–2013. *Obstet Gynecol* 2017;**130**:366–73.
4. Creanga AA, Berg CJ, Syverson C, Seed K, Bruce FC, Callaghan WM. Pregnancy-related mortality in the United States, 2006–2010. *Obstet Gynecol* 2015;**125**:5–12.
5. Knight MNM, Tuffnell D, Shakespeare J, Kenyon S. Kurinczuk JJ, on behalf of MBBRACE-UK. Saving lives, improving mothers' care – lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2013–2015. Oxford: National Perinatal Epidemiology Unit, University of Oxford; 2017;24–36.
6. Canobbio MM, Warnes CA, Aboulhosn J, et al. Management of pregnancy in patients with complex congenital heart disease: a scientific statement for healthcare professionals from the American Heart Association. *Circulation* 2017;**135**:e50–87.
7. Roos-Hesselink JW, Ruys TP, Stein JI, et al. Outcome of pregnancy in patients with structural or ischaemic heart disease:

results of a registry of the European Society of Cardiology. *Eur Heart J* 2013;**34**:657–65.
8. Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 Guidelines for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association task force on practice guidelines. *Circulation* 2008;**118**:e714–833.
9. Thorne S, MacGregor A, Nelson-Piercy C. Risks of contraception and pregnancy in heart disease. *Heart* 2006;**92**:1520–5.
10. Lindley KJ, Conner SN, Cahill AG, Madden T. Contraception and pregnancy planning in women with congenital heart disease. *Curr Treat Options Cardiovasc Med* 2015;**17**:50.
11. Siu SC, Sermer M, Colman JM, et al. Prospective multicenter study of pregnancy outcomes in women with heart disease. *Circulation* 2001;**104**:515–21.
12. Drenthen W, Boersma E, Balci A, et al. Predictors of pregnancy complications in women with congenital heart disease. *Eur Heart J* 2010;**31**:2124–32.
13. Silversides CK, Grewal J, Mason J, et al. Pregnancy outcomes in women with heart disease: the CARPREG II study. *J Am Coll Cardiol* 2018;**71**:2419–30.
14. Balci A, Sollie-Szarynska KM, van der Bijl AG, et al. Prospective validation and assessment of cardiovascular and offspring risk models for pregnant women with congenital heart disease. *Heart* 2014;**100**:1373–81.
15. Bedard E, Dimopoulos K, Gatzoulis MA. Has there been any progress made on pregnancy outcomes among women with pulmonary arterial hypertension? *Eur Heart J* 2009;**30**:256–65.
16. Kiely DG, Condliffe R, Webster V, et al. Improved survival in pregnancy and pulmonary hypertension using a multiprofessional approach. *BJOG* 2010;**117**:565–74.
17. Safdar Z. Pulmonary arterial hypertension in pregnant women. *Ther Adv Respir Dis* 2013;**7**:51–63.
18. Huang S, DeSantis ER. Treatment of pulmonary arterial hypertension in pregnancy. *Am J Health Syst Pharm* 2007;**64**:1922–6.
19. van Hagen IM, Roos-Hesselink JW. Aorta pathology and pregnancy. *Best Pract Res Clin Obstet Gynaecol* 2014;**28**:537–50.
20. Kim SY, Wolfe DS, Taub CC. Cardiovascular outcomes of pregnancy in Marfan's syndrome patients: a literature review. *Congenit Heart Dis* 2018;**13**:203–9.
21. Task force on the management of cardiovascular diseases during pregnancy of the European Society of Cardiology. Expert consensus document on management of cardiovascular diseases during pregnancy. *Eur Heart J* 2003;**24**:761–81.
22. Franklin WJ, Gandhi M. Congenital heart disease in pregnancy. *Cardiol Clin* 2012;**30**:383–94.
23. Stergiopoulos K, Shiang E, Bench T. Pregnancy in patients with pre-existing cardiomyopathies. *J Am Coll Cardiol* 2011;**58**:337–50.
24. Fett JD, Fristoe KL, Welsh SN. Risk of heart failure relapse in subsequent pregnancy among peripartum cardiomyopathy mothers. *Int J Gynaecol Obstet* 2010;**109**:34–6.
25. Elkayam U, Tummala PP, Rao K, et al. Maternal and fetal outcomes of subsequent pregnancies in women with peripartum cardiomyopathy. *N Engl J Med* 2001;**344**:1567–71.
26. Hilfiker-Kleiner D, Haghikia A, Masuko D, et al. Outcome of subsequent pregnancies in patients with a history of peripartum cardiomyopathy. *Eur J Heart Fail* 2017;**19**:1723–8.
27. Frishman WH, Elkayam U, Aronow WS. Cardiovascular drugs in pregnancy. *Cardiol Clin* 2012;**30**:463–91.
28. Lindley KJ, Conner SN, Cahill AG. Adult congenital heart disease in pregnancy. *Obstet Gynecol Surv* 2015;**70**:397–407.
29. Fernandes SM, Arendt KW, Landzberg MJ, Economy KE, Khairy P. Pregnant women with congenital heart disease: cardiac, anesthetic and obstetrical implications. *Expert Rev Cardiovasc Ther* 2010;**8**:439–48.
30. Arendt KW, Fernandes SM, Khairy P, et al. A case series of the anesthetic management of parturients with surgically repaired tetralogy of Fallot. *Anesth Analg* 2011;**113**:307–17.
31. Nishimura RA, Tajik AJ. The Valsalva maneuver-3 centuries later. *Mayo Clin Proc* 2004;**79**:577–8.
32. Nishimura RA, Tajik AJ. The Valsalva maneuver and response revisited. *Mayo Clin Proc* 1986;**61**:211–7.
33. Shnider SM, Abboud TK, Artal R, Henriksen EH, Stefani SJ, Levinson G. Maternal catecholamines decrease during labor after lumbar epidural anesthesia. *Am J Obstet Gynecol* 1983;**147**:13–5.
34. Jouppila P, Jouppila R, Hollmen A, Koivula A. Lumbar epidural analgesia to improve intervillous blood flow during labor in severe preeclampsia. *Obstet Gynecol* 1982;**59**:158–61.
35. Ramos-Santos E, Devoe LD, Wakefield ML, Sherline DM, Metheny WP. The effects of epidural anesthesia on the Doppler velocimetry of umbilical and uterine arteries in normal and hypertensive patients during active term labor. *Obstet Gynecol* 1991;**77**:20–6.
36. Robson S, Hunter S, Boys R, Dunlop W, Bryson M. Changes in cardiac output during epidural anaesthesia for caesarean section. *Anaesthesia* 1989;**44**:475–9.
37. Robson SC, Dunlop W, Boys RJ, Hunter S. Cardiac output during labour. *Br Med J (Clin Res Ed)* 1987;**295**:1169–72.
38. Cappiello E, O'Rourke N, Segal S, Tsen LC. A randomized trial of dural puncture epidural technique compared with the standard epidural technique for labor analgesia. *Anesth Analg* 2008;**107**:1646–51.
39. Chau A, Bibbo C, Huang CC, et al. Dural puncture epidural technique improves labor analgesia quality with fewer side effects compared with epidural and combined spinal epidural techniques: a randomized clinical trial. *Anesth Analg* 2017;**124**:560–9.
40. Halpern SH, Soliman A, Yee J, Angle P, Ioscovich A. Conversion of epidural labour analgesia to anaesthesia for Caesarean section: a prospective study of the incidence and determinants of failure. *Br J Anaesth* 2009;**102**:240–3.
41. Saberski LR, Kondamuri S, Osinubi OY. Identification of the epidural space: Is loss of resistance to air a safe technique? A review of the complications related to the use of air. *Reg Anesth* 1997;**22**:3–15.
42. Jaffe RA, Siegel LC, Schnittger I, Propst JW, Brock-Utne JG. Epidural air injection assessed by transesophageal echocardiography. *Reg Anesth* 1995;**20**:152–5.
43. Langesaeter E, Dragsund M, Rosseland LA. Regional anaesthesia for a Caesarean section in women with cardiac disease: a prospective study. *Acta Anaesthesiol Scand* 2010;**54**:46–54.
44. Arendt KWMJ, Tsen LT. Cardiovascular alterations in the parturient undergoing cesarean delivery with neuraxial anesthesia. *Exp Rev Obstet Gynecol* 2014;**7**:59–75.
45. Hamlyn EL, Douglass CA, Plaat F, Crowhurst JA, Stocks GM. Low-dose sequential combined spinal-epidural: an anaesthetic technique for caesarean section in patients with significant cardiac disease. *Int J Obstet Anesth* 2005;**14**:355–61.
46. Dresner M, Pinder A. Anaesthesia for caesarean section in women with complex cardiac disease: 34 cases using the Braun Spinocath spinal catheter. *Int J Obstet Anesth* 2009;**18**:131–6.
47. Abildgaard U, Sandset PM, Hammerstrom J, Gjestvang FT, Tveit A. Management of pregnant women with mechanical heart valve prosthesis: thromboprophylaxis with low molecular weight heparin. *Thromb Res* 2009;**124**:262–7.
48. Chan WS, Anand S, Ginsberg JS. Anticoagulation of pregnant women with mechanical heart valves: a systematic review of the literature. *Arch Intern Med* 2000;**160**:191–6.
49. Horlocker TT, Wedel DJ, Rowlingson JC, Enneking FK. Executive summary: 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**:102–5.
50. Gogarten W, Vandermeulen E, Van Aken H, Kozek S, Llau JV, Samama CM. Regional anaesthesia and antithrombotic agents:

recommendations of the European Society of Anaesthesiology. *Eur J Anaesthesiol* 2010;**27**:999–1015.
51. Vandermeulen E, Decoster J, Dewandre PY, Ickx BE, Vercauteren P, Verhamme P. Central neural blockade in patients with a drug-induced alteration of coagulation. Third edition of the Belgian Association for Regional Anaesthesia (BARA) guidelines. *Acta Anaesthesiol Belg* 2011;**62**:175–91.
52. Breivik H, Bang U, Jalonen J, Vigfusson G, Alahuhta S, Lagerkranser M. Nordic guidelines for neuraxial blocks in disturbed haemostasis from the Scandinavian Society of Anaesthesiology and Intensive Care Medicine. *Acta Anaesthesiol Scand* 2010;**54**:16–41.
53. Fonseca NM, Alves RR, Pontes JP. SBA recommendations for regional anesthesia safety in patients taking anticoagulants. *Braz J Anesthesiol* 2014;**64**:1–15.
54. Horlocker TT, Vandermeuelen E, Kopp SL, Gogarten W, Leffert LR, Benzon LR. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine evidence-based guidelines (Fourth Edition). *Reg Anesth Pain Med* 2018;**43**:263–309.
55. Leffert L, Butwick A, Carvalho B, 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**:928–44.
56. Ngan Kee WD, Khaw KS, Ma KC, Wong AS, Lee BB, Ng FF. Maternal and neonatal effects of remifentanil at induction of general anesthesia for cesarean delivery: a randomized, double-blind, controlled trial. *Anesthesiology* 2006;**104**:14–20.
57. Heesen M, Klohr S, Hofmann T, et al. Maternal and foetal effects of remifentanil for general anaesthesia in parturients undergoing caesarean section: a systematic review and meta-analysis. *Acta Anaesthesiol Scand* 2013;**57**:29–36.
58. Wadsworth R, Greer R, MacDonald JM, Vohra A. The use of remifentanil during general anaesthesia for caesarean delivery in two patients with severe heart dysfunction. *Int J Obstet Anesth* 2002;**11**:38–43.
59. Manullang TR, Chun K, Egan TD. The use of remifentanil for cesarean section in a parturient with recurrent aortic coarctation. *Can J Anaesth* 2000;**47**:454–9.
60. Orme RM, Grange CS, Ainsworth QP, Grebenik CR. General anaesthesia using remifentanil for caesarean section in parturients with critical aortic stenosis: a series of four cases. *Int J Obstet Anesth* 2004;**13**:183–7.
61. Ouzounian JG, Elkayam U. Physiologic changes during normal pregnancy and delivery. *Cardiol Clin* 2012;**30**:317–29.
62. Goland S, Modi K, Bitar F, et al. Clinical profile and predictors of complications in peripartum cardiomyopathy. *J Card Fail* 2009;**15**:645–50.
63. Mhyre JM, D'Oria R, Hameed AB, et al. The maternal early warning criteria: a proposal from the national partnership for maternal safety. *Obstet Gynecol* 2014;**124**:782–6.
64. Tanous D, Siu SC, Mason J, et al. B-type natriuretic peptide in pregnant women with heart disease. *J Am Coll Cardiol* 2010;**56**:1247–53.
65. Resnik JL, Hong C, Resnik R, et al. Evaluation of B-type natriuretic peptide (BNP) levels in normal and preeclamptic women. *Am J Obstet Gynecol* 2005;**193**:450–4.
66. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 106: Intrapartum fetal heart rate monitoring: nomenclature, interpretation, and general management principles. *Obstet Gynecol* 2009;**114**:192–202.
67. Bullens LM, Heimel PJV, van der Hout-van der Jagt MB, Oei SG. Interventions for intrauterine resuscitation in suspected fetal distress during term labor: a systematic review. *Obstet Gynecol Surv* 2015;**70**:524–39.
68. Ying Y-K, Tejani NA. Case reports: angina pectoris as a complication of ritodrine hydrochloride therapy in premature labor. *Obstet Gynecol* 1982;**60**:385–8.
69. Ron-El R, Caspi E, Herman A, Schreyer P, Algom M, Schlezinger Z. Unexpected cardiac pathology in pregnant women treated with beta-adrenergic agents (ritodrine). *Obstet Gynecol* 1983;**61**:10S–1S.
70. Langesæter E, Rosseland LA, Stubhaug A. Hemodynamic effects of oxytocin during cesarean delivery. *Int J Gynecol Obstet* 2006;**95**:46–7.
71. Langesaeter E, Rosseland LA, Stubhaug A. Haemodynamic effects of repeated doses of oxytocin during caesarean delivery in healthy parturients. *Br J Anaesth* 2009;**103**:260–2.
72. Archer TL, Knape K, Liles D, Wheeler AS, Carter B. The hemodynamics of oxytocin and other vasoactive agents during neuraxial anesthesia for cesarean delivery: findings in six cases. *Int J Obstet Anesth* 2008;**17**:247–54.
73. Svanström MC, Biber B, Hanes M, Johansson G, Näslund U. Signs of myocardial ischaemia after injection of oxytocin: a randomized double-blind comparison of oxytocin and methylergometrine during caesarean section. *Br J Anaesth* 2008;**100**:683–9.
74. Bolton TJ, Randall K, Yentis SM. Effect of the confidential enquiries into maternal deaths on the use of Syntocinon® at caesarean section in the UK. *Anaesthesia* 2003;**58**:277–9.
75. Secher NJ, Andersen LH. Changes in the pattern of regional pulmonary blood flow after PGF2 infusion in pregnant women. *Cardiovasc Res* 1977;**11**:26–30.
76. Partridge BL, Key T, Reisner LS. Life-threatening effects of intravascular absorption of PGF2 alpha during therapeutic termination of pregnancy. *Anesth Analg* 1988;**67**:1111–3.
77. Lin YH, Seow KM, Hwang JL, Chen HH. Myocardial infarction and mortality caused by methylergonovine. *Acta Obstet Gynecol Scand* 2005;**84**:1022.
78. Secher NJ, Arnsbo P, Wallin L. Haemodynamic effects of oxytocin (syntocinon) and methyl ergometrine (methergin) on the systemic and pulmonary circulations of pregnant anaesthetized women. *Acta Obstet Gynecol Scand* 1978;**57**: 97–103.
79. Spitzer Y, Weiner MM, Beilin Y. Cesarean delivery in a parturient with left ventricular noncompaction complicated by acute pulmonary hypertension after methylergonovine administration for postpartum hemorrhage. *A A Case Rep* 2015;**4**:166–8.
80. Elbohoty AEH, Mohammed WE, Sweed M, Bahaa Eldin AM, Nabhan A, Abd-El-Maeboud KHI. Randomized controlled trial comparing carbetocin, misoprostol, and oxytocin for the prevention of postpartum hemorrhage following an elective cesarean delivery. *Int J Gynecol Obstet* 2016;**134**:324–8.
81. Quibel T, Ghout I, Goffinet F, et al. Active management of the third stage of labor with a combination of oxytocin and misoprostol to prevent postpartum hemorrhage: a randomized controlled trial. *Obstet Gynecol* 2016;**128**:805–11.
82. Silversides CK, Harris L, Haberer K, Sermer M, Colman JM, Siu SC. Recurrence rates of arrhythmias during pregnancy in women with previous tachyarrhythmia and impact on fetal and neonatal outcomes. *Am J Cardiol* 2006;**97**:1206–12.
83. Page RL, Joglar JA, Caldwell MA, et al. 2015 ACC/AHA/HRS Guideline for the management of adult patients with supraventricular tachycardia: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines and the Heart Rhythm Society. *Circulation* 2016;**133**:e506–74.
84. Jeejeebhoy FM, Zelop CM, Lipman S, et al. Cardiac arrest in pregnancy: a scientific statement from the American Heart Association. *Circulation* 2015;**132**:1747–73.
85. Lipman S, Cohen S, Einav S, et al. The Society for Obstetric Anesthesia and Perinatology consensus statement on the management of cardiac arrest in pregnancy. *Anesth Analg* 2014;**118**:1003–16.
86. Rose CH, Faksh A, Traynor KD, Cabrera D, Arendt KW, Brost BC. Challenging the 4- to 5-minute rule: from perimortem cesarean to resuscitative hysterotomy. *Am J Obstet Gynecol* 2015;**213**:653–6. e1.