

Management of acute cardiovascular complications in pregnancy

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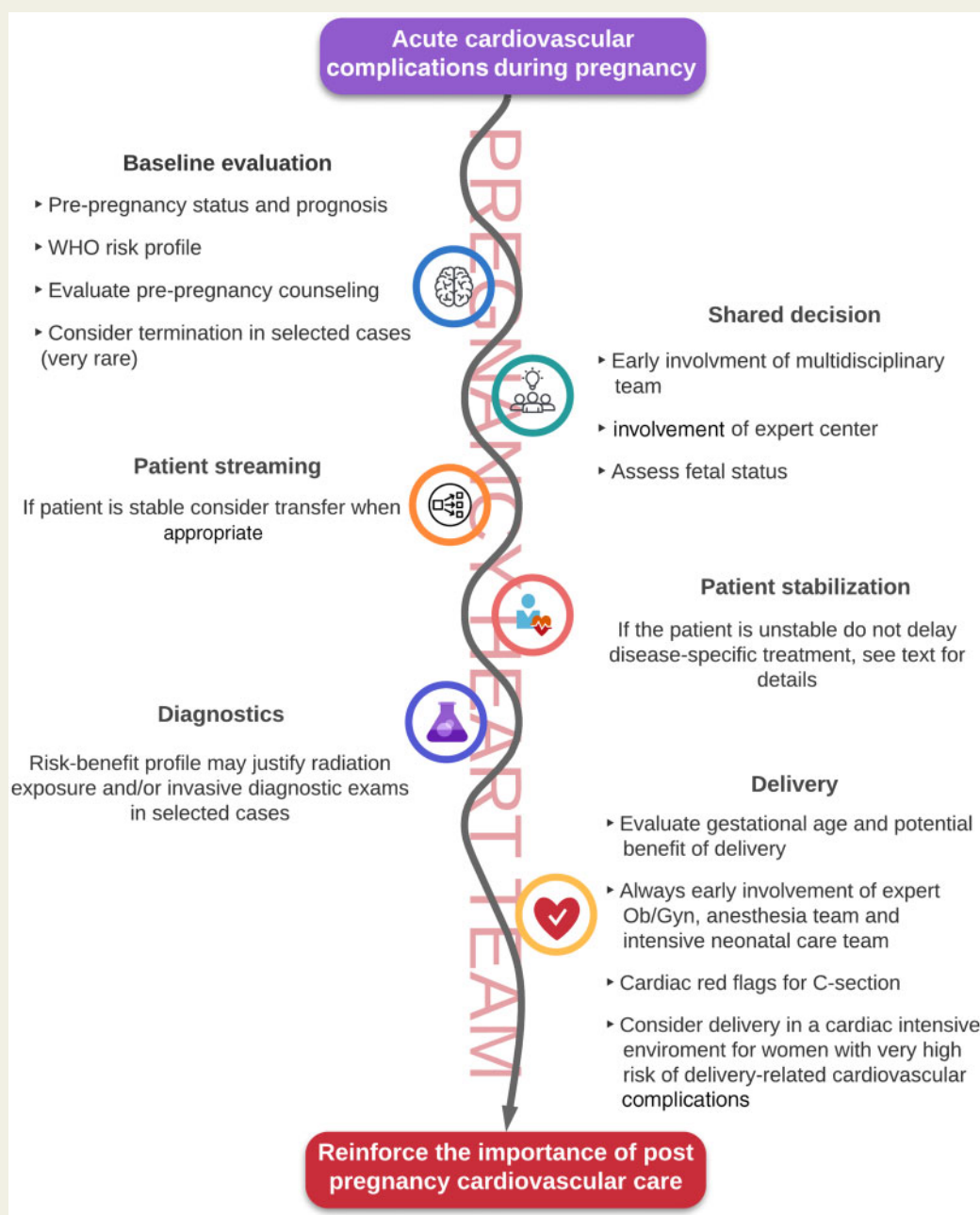
The growing population of women with heart disease of reproductive age has been associated with an increasing number of high-risk pregnancies. Pregnant women with heart disease are a very heterogeneous population, with different risks for maternal cardiovascular, obstetric, and foetal complications. Adverse cardiovascular events during pregnancy pose significant clinical challenges, with uncertainties regarding diagnostic and therapeutic approaches potentially compromising maternal and foetal health. This review summarizes best practice for the treatment of common cardiovascular complications during pregnancy, based on expert opinion, current guidelines, and available evidence. Topics covered include heart failure (HF), arrhythmias, coronary artery disease, aortic and thromboembolic events, and the management of mechanical heart valves during pregnancy. Cardiovascular pathology is the leading cause of non-obstetric morbidity and mortality during pregnancy in developed countries. For women with pre-existing cardiac conditions, preconception counselling and structured follow-up during pregnancy are important measures for reducing the risk of acute cardiovascular complications during gestation and at the time of delivery. However, many women do not receive pre-pregnancy counselling often due to gaps in what should be lifelong care, and physicians are increasingly encountering pregnant women who present acutely with cardiac complications, including HF, arrhythmias, aortic events, coronary syndromes, and bleeding or thrombotic events. This review provides a summary of recommendations on the management of acute cardiovascular complication during pregnancy, based on available literature and expert opinion. This article covers the diagnosis, risk stratification, and therapy and is organized according to the clinical presentation and the type of complication, providing a reference for the practicing cardiologist, obstetrician, and acute medicine specialist, while highlighting areas of need and potential future research.

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Graphical Abstract



Multidisciplinary and expert team ('pregnancy heart team') should be ideally involved early in the care of a pregnant woman presenting with an acute cardiovascular complication during gestation. Proposed staged approach to expedite risk stratification, diagnosis and management is summarised in the graphical abstract.

Keywords

Pregnancy • Heart failure • Valvular heart disease • Congenital heart disease • Arrhythmias
• Aortic dissection • Acute coronary syndrome

Introduction

The number of pregnancies and deliveries in women with cardiovascular conditions has been growing for several decades, largely due to the increasing population of adults surviving with congenital heart disease (CHD) and the rising average age of pregnant women in developed countries.^{1–3} Cardiovascular diseases are the most common cause of non-obstetric death during pregnancy,⁴ whereas cardiac patients requiring emergency hospitalization during pregnancy (high dependency of intensive care, 6.4/1000 pregnancies) have a significant mortality of 5%.^{5,6} There is limited evidence to guide the management of pregnant women with cardiovascular disease, with most data deriving from retrospective series or large international registries; therefore, expert opinion remains important in formulating clinical recommendations.^{4,7}

Cardiovascular complications during pregnancy often occur outside tertiary referral centres and pose significant challenges to practitioners in cardiac and emergency medicine.⁷ Our paper is aimed at practitioners who may encounter such patients in emergency, non-tertiary settings, and discusses the diagnosis and management of acute cardiovascular complications during pregnancy, based on expert opinion and best evidence (*Graphical abstract*).^{4,7,8}

Cardiovascular physiology during pregnancy

Pregnancy imposes a significant, dynamic, and progressive overload to the cardiovascular system, with a rising cardiac output (CO) and increasing metabolic demands to support the foetus and the placenta (*Figure 1*). Physiological adaptation to pregnancy includes progressive reduction of systemic and pulmonary vascular resistance to accommodate for the increasing maternal CO. Augmentation of stroke volume takes place early during gestation, whereas increased heart rate (HR) is a more predominant mechanism during the second and third

trimesters (please refer to [Supplementary material online, Appendix S1](#) for additional details).

Risk stratification and counselling

Women of reproductive age with a history of heart disease or aortic pathology should be carefully assessed and should receive preconception counselling, to discuss the risk of cardiovascular, obstetric, and neonatal complications.^{4,9,10} Furthermore, recurrence of CHD in the foetus and guidance on best timing of having children and lifestyle choices (such as optimal body mass index and regular exercise to minimize risk) must be addressed. Preconception counselling, therefore, can touch upon sensitive subjects and is ideally performed by experienced physicians.^{10,11}

The World Health Organization (WHO) developed a risk-based classification of cardiac diseases during pregnancy, which is based on expert consensus and available evidence.^{3,12} A modified version of the WHO classification (mWHO) has been validated prospectively using the Registry Of Pregnancy And Cardiac disease (ROPAC), resulting in a robust tool for clinicians managing women with cardiovascular pathology during pregnancy (*Table 1*).¹² Maternal features and other risk factors associated with unfavourable maternal, obstetric and neonatal outcomes are shown in [Supplementary material online, Table S1](#).^{11,13} Other important validated tools for risk assessment [Cardiac Disease in Pregnancy Study, CARPREG; Zwangerschap bij Aangeboren HARTAfwijkingen (pregnancy with CHD), ZAHARA] during pregnancy are also useful in the acute setting, to rapidly risk stratify pregnant women and identify high-risk clinical scenarios, e.g. women with very high or prohibitive risks who should be offered termination or early delivery, depending on the time of presentation ([Supplementary material online, Table S1](#)). Pregnancy termination for cardiac reason is rare and should be considered after multidisciplinary evaluation in a tertiary and expert referral centre. Advice and assistance from a specialist centre should always be sought, aiming for early transfer if safe to do so.¹⁴

Acute cardiovascular complications during pregnancy

Arrhythmias

New-onset or recurrent supraventricular tachyarrhythmias are not uncommon in pregnant women with structural heart disease or advanced age,^{15,16} while complex ventricular tachyarrhythmias or symptomatic bradycardia are rare. Paroxysmal atrial fibrillation is associated with increased maternal morbidity and mortality, and an underlying cause for the arrhythmia should always be sought.¹⁵ In women with CHD, supraventricular tachycardias are also associated with increased maternal morbidity and mortality.¹⁶

Management of supraventricular arrhythmias

Figure 2 summarizes indications for the acute management of supraventricular tachycardias during pregnancy. Haemodynamically unstable patients, especially those with complex anatomy, ventricular dysfunction, or pulmonary hypertension, should receive direct current cardioversion (DCCV) as soon as feasible; this procedure can be

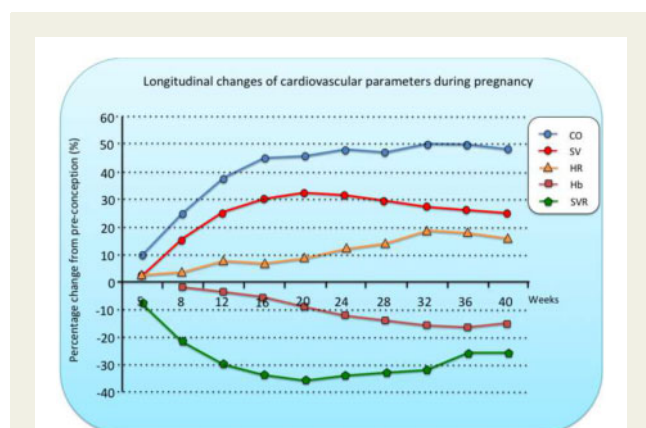


Figure 1 Longitudinal percent change in major cardiovascular variables during pregnancy, compared to pre-gestational values. CO, cardiac output; Hb, haemoglobin; HR, heart rate; SV, stroke volume; SVR, systemic vascular resistance.

Table 1 Modified World Health Organization classification of heart disease during pregnancy

	mWHO I	mWHO II	mWHO II-III	mWHO III	mWHO IV
Diagnosis	Small or mild Pulmonary stenosis Patent ductus arteriosus Mitral valve prolapse Successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, anomalous pulmonary venous drainage) Atrial or ventricular ec- topic beats, isolated	Unoperated atrial or ventricular septal defect Repaired tetralogy of Fallot Most arrhythmias (supraventricular arrhythmias) Turner syndrome with- out aortic dilatation	Mild left ventricular im- pairment (EF > 45%) Hypertrophic cardiomyopathy Native or tissue valve disease not consid- ered WHO I or IV (mild mitral stenosis, moderate aortic stenosis) Marfan or other HTAD syndrome without aortic dilatation Aorta <45 mm in bicus- pid aortic valve pathology Repaired coarctation Atrioventricular septal defect	Moderate left ventricu- lar impairment (EF 30–45%) Previous peripartum cardiomyopathy with- out any residual left ventricular impairment Mechanical valve Systemic right ventricle with good or mildly decreased ventricular function Fontan circulation. If otherwise the patient is well and the cardiac condition uncomplicated Unrepaired cyanotic heart disease Other complex heart disease Moderate mitral stenosis Severe asymptomatic aortic stenosis Moderate aortic dilata- tion (40–45 mm in Marfan syndrome or other HTAD; 45– 50 mm in bicuspid aortic valve, Turner syndrome ASI 20– 25 mm/m ² , tetralogy of Fallot <50 mm) Ventricular tachycardia	Pulmonary arterial hypertension Severe systemic ven- tricular dysfunction (EF <30% or NYHA Class III–IV) Previous peripartum cardiomyopathy with any residual left ven- tricular impairment Severe mitral stenosis Severe symptomatic aortic stenosis Systemic right ventricle with moderate or se- verely decreased ven- tricular function Severe aortic dilatation (>45 mm in Marfan syndrome or other HTAD, >50 mm in bi- cuspid aortic valve, Turner syndrome ASI >25 mm/m ² , tetralogy of Fallot >50 mm) Vascular Ehlers–Danlos Severe (re)coarctation Fontan with any complication
Risk	No detectable increased risk of ma- ternal mortality and no/mild increased risk in morbidity	Small increased risk of maternal mortality or moderate increase in morbidity	Intermediate increased risk of maternal mor- tality or moderate to severe increase in morbidity	Significantly increased risk of maternal mor- tality or severe morbidity	Extremely high risk of maternal mortality or severe morbidity
Maternal cardiac event rate (%)	2.5–5	5.7–10.5	10–19	19–27	40–100
Counselling: Pregnancy advisable	Yes	Yes	Yes	Yes: expert counselling required	No: pregnancy contra- indicated: if preg- nancy occurs, termination should be discussed
Care during pregnancy	Local hospital	Local hospital	Referral hospital	Expert centre for preg- nancy and cardiac disease	Expert centre for pregnancy and car- diac disease

Continued

Table I Continued

	mWHO I	mWHO II	mWHO II-III	mWHO III	mWHO IV
Minimal follow-up visits during pregnancy	Once or twice	Once per trimester	Bimonthly	Monthly or bimonthly	Monthly
Location of delivery	Local hospital	Local hospital	Referral hospital	Expert centre for pregnancy and cardiac disease	Expert centre for pregnancy and cardiac disease

From Regitz-Zagrosek et al.⁴
ASI, aortic size index; EF, ejection fraction; HTAD, heritable thoracic aortic disease; mWHO, modified World Health Organization; NYHA, New York Heart Association; WHO, World Health Organization.

performed with minimal sedation and is safe for the foetus and is generally well-tolerated in pregnancy (Figure 2).^{16,17}

Atrioventricular node-dependent arrhythmias can be terminated using vagal manoeuvres, rapid adenosine challenge, or beta-blockers (Figure 2).⁴ In refractory cases, Class I antiarrhythmic drugs may be considered after consultation with a cardiac electrophysiologist providing that there is no significant ventricular dysfunction or a complex structural congenital heart defect.¹² Amiodarone has been associated with adverse foetal effect (such as thyroid abnormalities) and it is usually reserved for severe cases refractory to other treatment.¹⁸

Atrial fibrillation or atrial flutter causing haemodynamic instability or foetal compromise also requires emergency DCCV (Figure 2). Short-term systemic anticoagulation with weight-adjusted dosing of low molecular weight heparin (LMWH) should also be considered.^{19,20}

Although pharmacological cardioversion may be appropriate in women without complex structural heart disease or ventricular dysfunction, it is usually carried out in tertiary referral centres by expert operators. Direct current cardioversion is the safe alternative in the majority of cases. Pre-DCCV (3-week) anticoagulation or transoesophageal echocardiography (TOE)-guided early cardioversion should be considered for longstanding episodes (>48 h)⁴ in anticoagulated-naïve patients, and in patients with moderate or complex CHD (Figure 2 and Supplementary material online, Table S2).^{4,19,21}

Long-term anticoagulation is usually not necessary (beyond the periprocedural cardioversion phase) in women with a low CHA₂DS₂-VAsC score (<1, discarding the obligatory female gender), the absence of mitral stenosis and/or severe left atrial dilatation (or spontaneous smoke/contrast effect on echocardiography), or structurally normal hearts (Figure 2).¹⁹ In all other cases (especially women with complex congenital heart lesions, including patients with the Fontan circulation), long-term full-dose anticoagulation with weight-adjusted dose of LMWH may be required. Direct oral anticoagulants are contraindicated in pregnancy.⁴

A rate control strategy may be appropriate in selected pregnant women with high risk of recurrence (e.g. rheumatic heart disease, with severe left atrial dilatation or history of multiple arrhythmia recurrences).¹⁹ Long-term rate control is usually achieved with a beta-blocker, verapamil, or rarely, digoxin.⁴

In any case long-term management should be discussed and agreed with an expert centre in pregnancy and heart disease.⁴

Catheter ablation of supraventricular arrhythmias during pregnancy is feasible and can be performed (in expert centres) with low risk to the mother and the foetus but is reserved for selected cases with recurrent arrhythmias refractory to medication, usually after the first trimester.²⁰

Management of ventricular arrhythmias

Complex ventricular arrhythmias, especially at the end of the third trimester or postpartum, in women without a history of heart disease, should raise the suspicion of cardiomyopathy [including peripartum cardiomyopathy (PPCM)], right ventricular infundibular tachycardia (which is the most common type of ventricular tachycardia in young pregnant women with structurally normal heart), or inherited arrhythmogenic syndromes (e.g. long QT syndrome, Brugada syndrome). Ventricular tachycardia poses complex diagnostic and therapeutic challenges during pregnancy and requires a multidisciplinary approach in expert centres.

Sustained ventricular arrhythmias typically require prompt DCCV, especially in women with signs of haemodynamic or foetal compromise, and those with complex disease or ventricular dysfunction.⁴ Foetal monitoring and early consultation and transfer (when safe) to an expert centre is recommended for further investigations and treatment, including multidisciplinary discussion regarding early delivery if appropriate. All pregnant women with ventricular tachycardia should be evaluated by a clinical electrophysiologist.

Maternal cardiac arrest

Although the basic principles of resuscitation for cardiac arrest apply to pregnant women (hence, formal resuscitation guidelines should be followed), there are important differences and adjustment that should be kept in mind.^{22,23}

Maternal cardiac arrest can lead to both maternal and foetal death as the uterus and placenta are poorly perfused during cardiogenic shock, and therefore, no blood is provided to the foetus. In women at the late stages of gestation (as testified by a uterus palpable above the umbilical line), emergency caesarean section should be considered when initial resuscitation attempts fail (within 4 min of cardiac arrest), as a means of increasing the chances of survival for both the mother and foetus.²² If this is not feasible (e.g. the resuscitation team is not able to perform caesarean delivery, hostile environment), rapid maternal transfer to the appropriate clinical setting with uninterrupted resuscitation is strongly recommended.²²

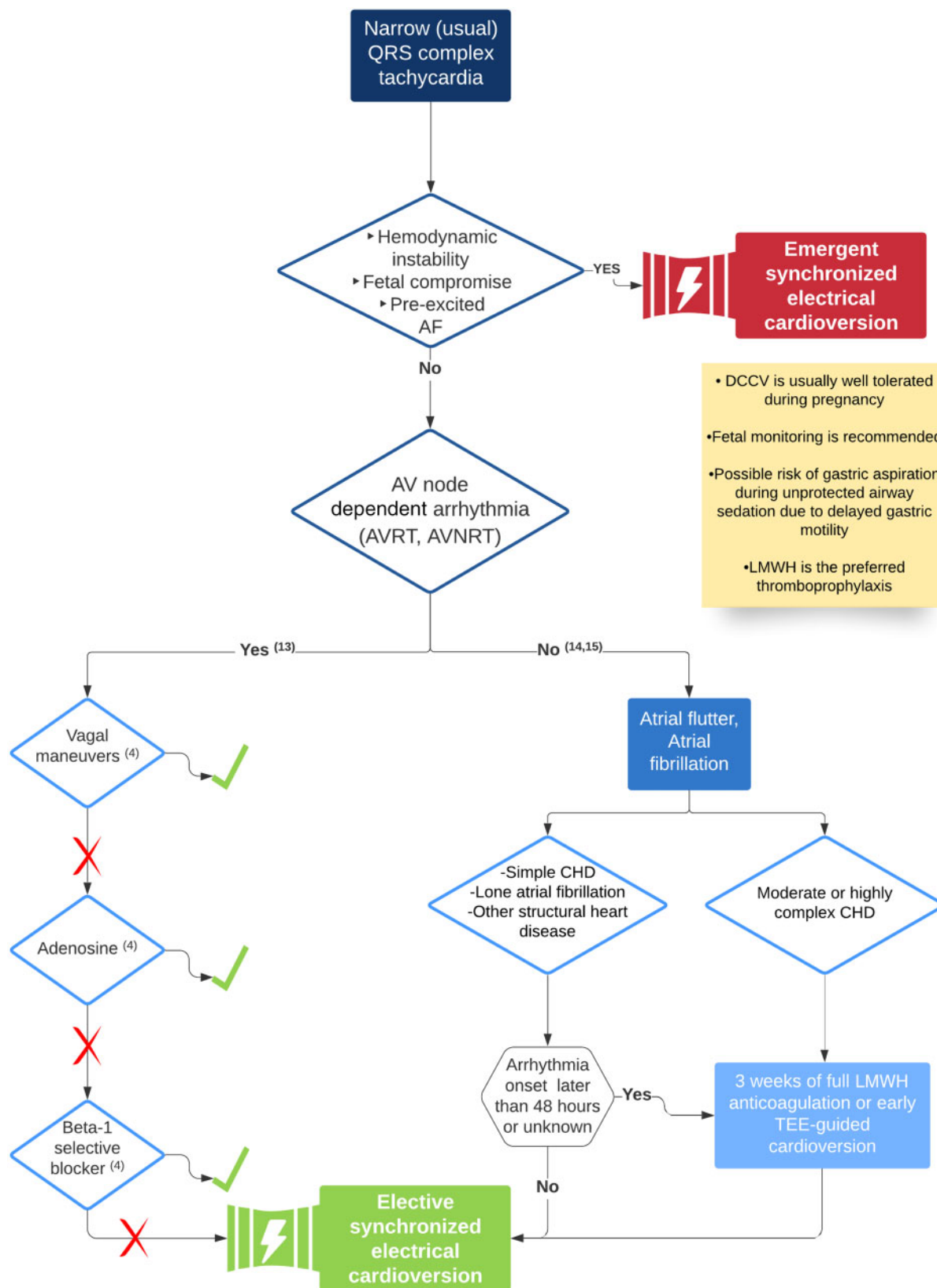


Figure 2 Suggested approach to supraventricular arrhythmias during pregnancy. AVRT, atrioventricular re-entrant tachycardia; AVNRT, atrioventricular nodal re-entrant tachycardia; CHD, congenital heart disease; LMWH, low molecular weight heparin; TOE, transoesophageal echocardiography.

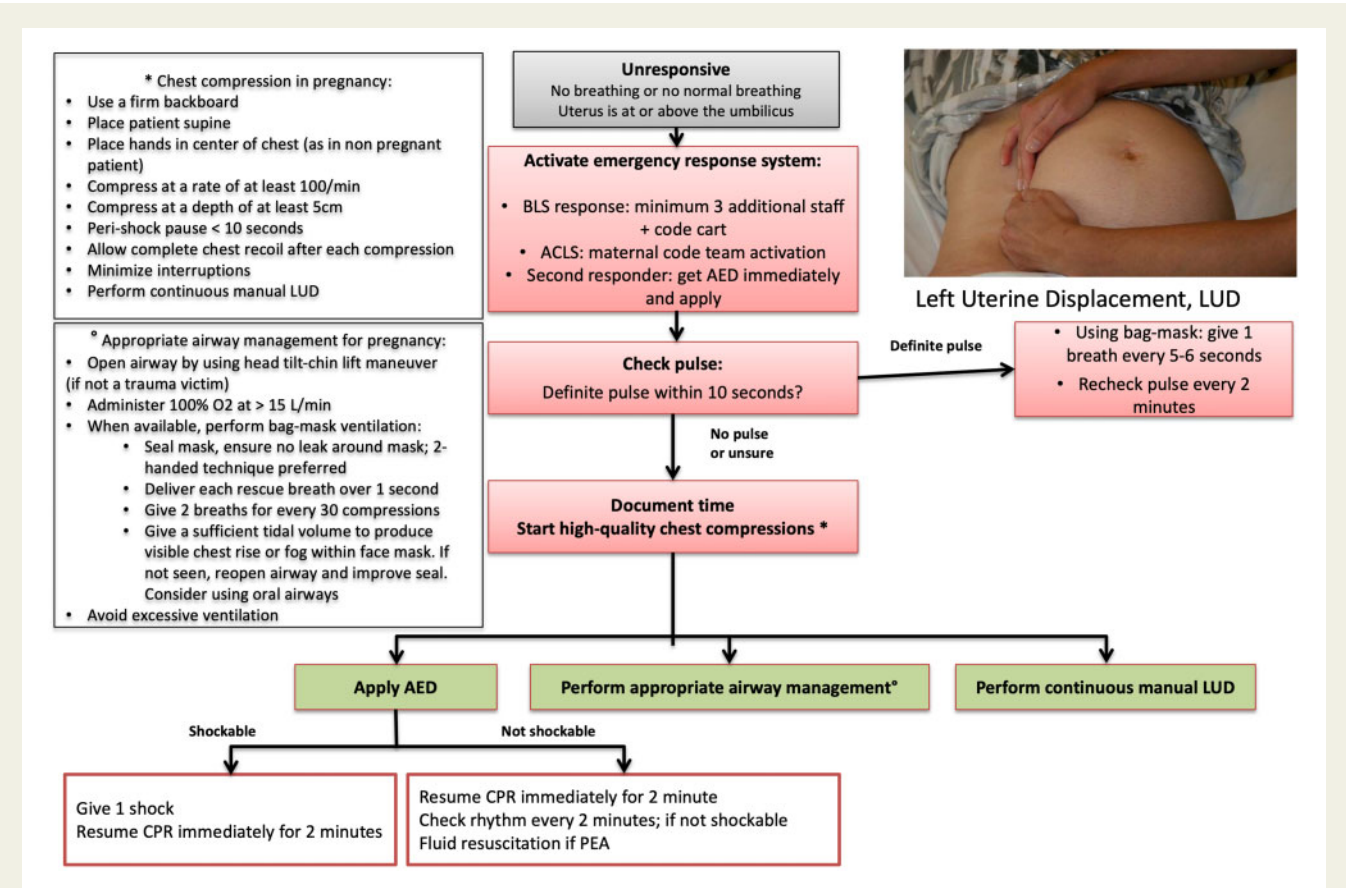


Figure 3 Suggested protocol for maternal cardiac arrest: basic life support. ACLS, advanced cardiac life support; AED, automatic external defibrillator; BLS, basic life support; CPR, cardiopulmonary resuscitation; LUD, left uterine displacement; PEA, pulseless electrical activity. Modified from Jeejeebhoy et al.²²

Figure 3 summarizes the main recommendations on cardiac resuscitation during pregnancy. Manual displacement of the uterus to the left (in patients with standard viscera and atrial situs) can increase systemic venous return by decompressing the inferior vena cava.²² Additional actions necessary for the resuscitation of pregnant women are summarized in Figure 4 and include early involvement of an expert resuscitation team, including an obstetrician and a neonatologist, with rapid transfer to an appropriate high-intensity care facility.

Acute heart failure

Acute heart failure (HF) during pregnancy can be secondary to a pre-existing cardiomyopathy, CHD, PPCM, stress/toxic cardiomyopathy, severe valvular heart disease, or myocardial ischaemia due to coronary artery dissection or atherosclerosis.²⁴ The delivery and postpartum are particularly sensitive periods due to rapid volume shifts, hormonal changes, and increased ventricular afterload.

New-onset HF presenting in pregnancy may have a rapid onset and progression requiring early diagnosis and prompt management. The diagnosis of HF during pregnancy can be challenging because many of the signs and symptoms may be misinterpreted as ‘normal’ effects of late pregnancy, including dyspnoea, orthopnoea, fatigue, tachycardia, leg oedema, and a third heart sound/gallop on auscultation.

Serum biomarkers and non-invasive imaging can help establish the diagnosis. A diagnostic algorithm for suspected HF during pregnancy is presented in Figure 5.⁴ The general cardiologist is usually involved in establishing the diagnosis, cause, and initial treatment (e.g. diuretics and/or arrhythmia termination, Figure 5).

Medical treatment of HF in pregnancy is complex because of the teratogenic effect of many commonly used HF medications, which must be avoided (including angiotensin-converting enzyme inhibitors, aldosterone antagonists, neprilysin inhibitors, sodium-glucose co-transporter 2 inhibitors) (Figure 5).⁴ Loop diuretics, such as furosemide, are considered safe in pregnancy and should be introduced early to control congestion and improve symptoms in pregnant women presenting with HF. Acute vasodilatation, when required, may be obtained with nitroglycerine or nitroprusside. HR control may be of some advantage, in particular in women with supraventricular arrhythmias or mitral stenosis. Inotropes can be used in the setting of a ‘wet and cold’ clinical phenotype with severe ventricular dysfunction; caution should be used in women with PPCM (risk of a toxic effect triggering ventricular arrhythmias) (Figure 5). There is little evidence to support the choice of inotropes in this setting. Pregnancy is typically associated with reduced systemic vascular resistance and pure inodilators may result in excessive hypotension that should be

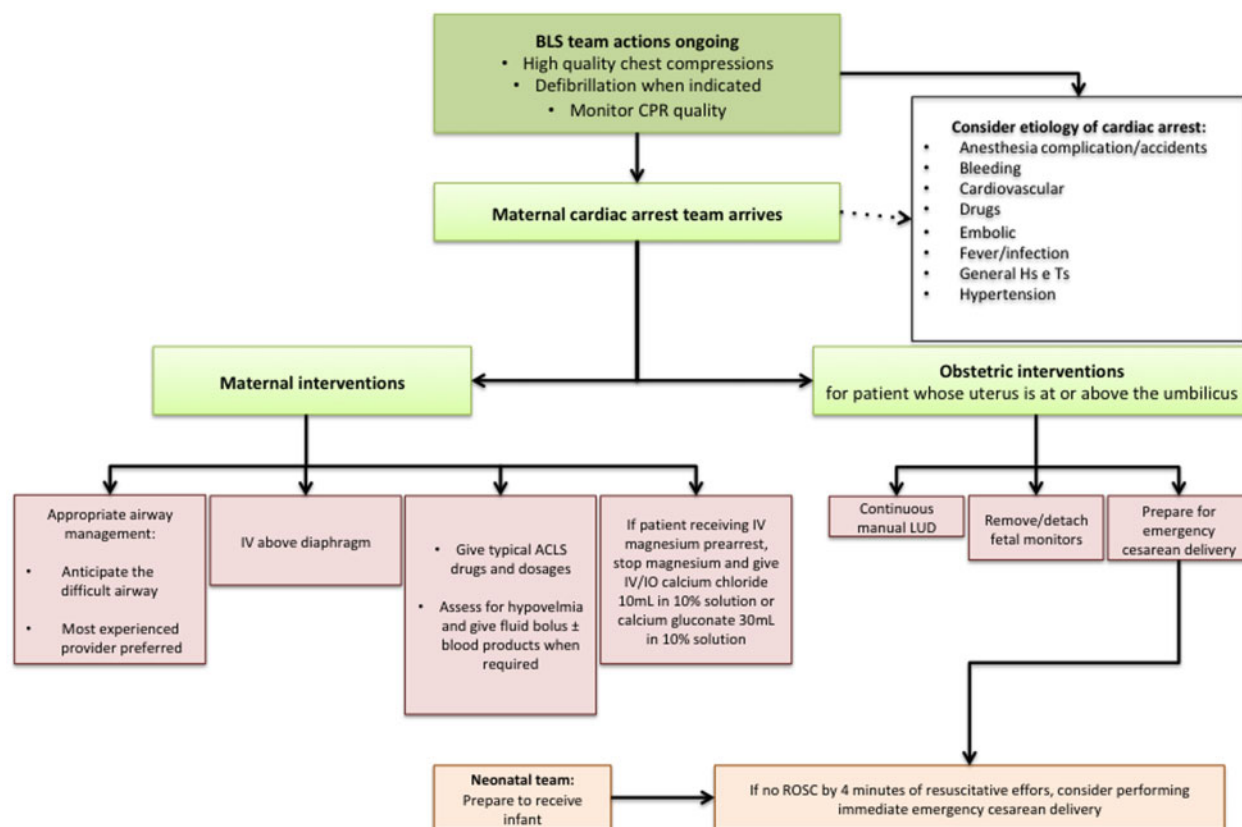


Figure 4 Suggested protocol for maternal cardiac arrest: advanced life support including potential role for emergency caesarean delivery. ACLS, advanced cardiac life support; BLS, basic life support; LUD, left uterine displacement; ROSC, return of spontaneous circulation. Modified from Jeejeebhoy *et al.*²²

counter-balanced by a combination with vasoconstrictors (Figure 5). Foetal monitoring is strongly advised in all cases. In selected women with valvular or CHD (e.g. aortic or mitral stenosis, bioprosthetic valve dysfunction in the aortic or mitral position), failing medical therapies, transcatheter procedures in a centre with technical expertise, and a pregnancy and heart disease service may be considered.²⁵

All women with suspected HF should be referred to an expert centre with an established multidisciplinary pregnancy and heart disease team, with a surgical and mechanical circulatory/transplant program as back-up (Figure 5).⁴

Acute aortic events

Although rare, acute aortic events, such as aortic dissection or rupture, are relatively more common in pregnant women compared to age-matched non-pregnant controls and are associated with significant morbidity and mortality.^{9,26} Risk factors for such complications are inherited connective tissue and vascular disorders, bicuspid aortic valve with severe ascending aortic dilatation, uncontrolled hypertension, and aortic coarctation.²⁷ Preconception diagnosis and expert counselling are mandatory to avoid high-risk women pursuing pregnancy without adequate risk assessment and treatment. On occasion,

however, the diagnosis may be established during pregnancy, at the time of an acute aortic event.

High-risk periods include the third trimester and delivery/postpartum. For the general cardiologist, a high level of awareness is required in the evaluation of any pregnant woman with signs or symptoms of dissection (chest and/or scapular pain, haemodynamic instability, abnormal peripheral arterial pulses, pericardial effusion, new-onset aortic regurgitation, acute coronary syndrome, or acute cerebrovascular event). In case of clinical suspicion, an emergency computed tomography (CT) scan is strongly advised (with abdominal shielding, if feasible and recommended). Alternatively, cardiac magnetic resonance may be used in stable cases, if promptly available.⁴ Upon clinical confirmation of aortic dissection, rapid referral to a tertiary centre is required. In haemodynamically stable patients, blood pressure control can be achieved using a beta-blocker, nitroglycerine/nitroprusside, and adequate pain management, with continuous foetal monitoring.

Type A aortic dissection is a surgical emergency. Associated maternal mortality rate is similar to the general population, but the risk of foetal loss is significant (30–40%).²⁸ Decision on whether to perform emergent caesarean delivery before surgery requires urgent multidisciplinary team discussion (including a surgeon, obstetrician, neonatologist, anaesthesiologist, cardiologist) involving the patient

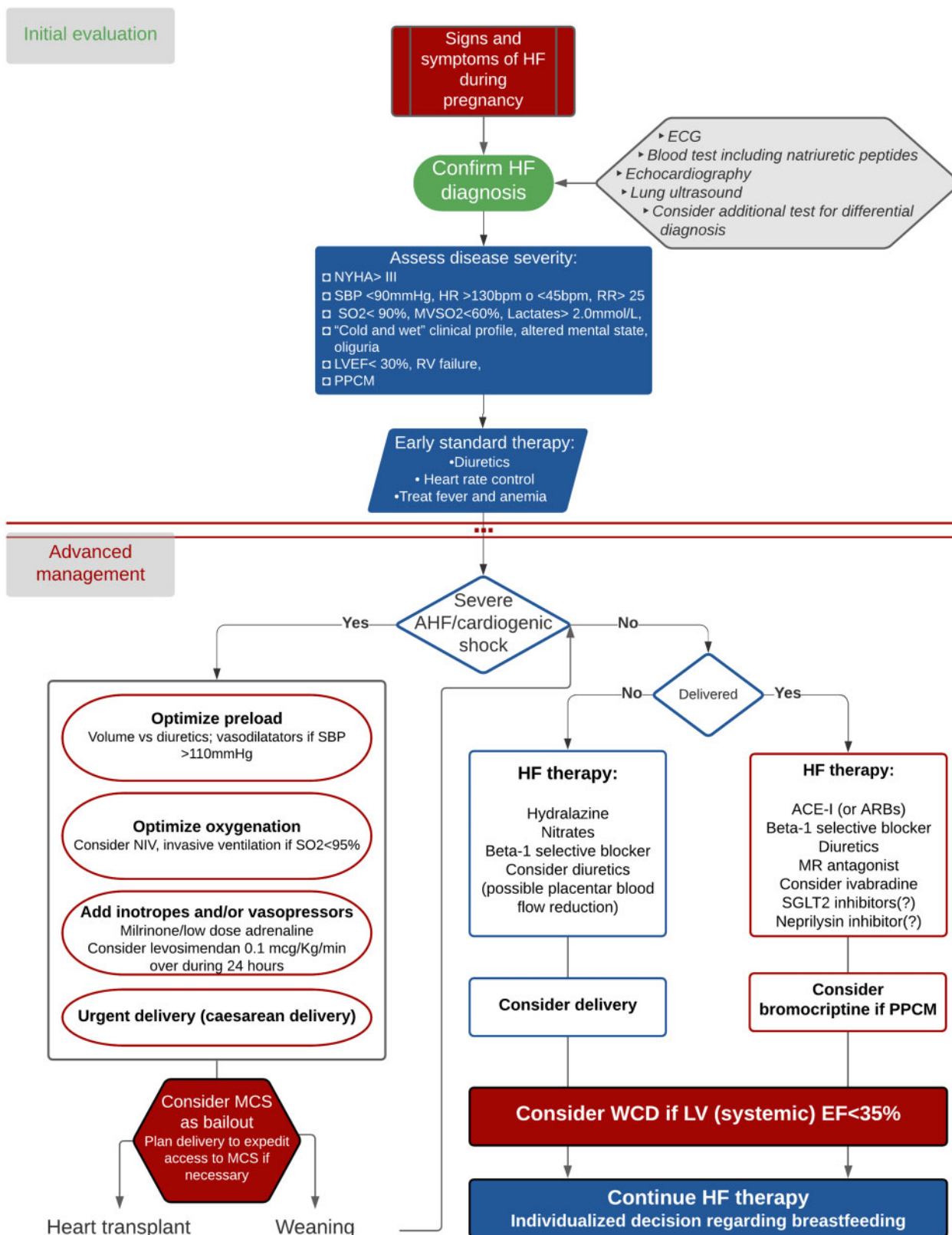


Figure 5 Suggested approach to heart failure during pregnancy. ACE-I, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker; AHF, acute heart failure; HR, heart rate; LVEF, left ventricular ejection fraction; MCS, mechanical circulatory support; MR, mineralocorticoid receptor; NIV, non-invasive ventilation; NYHA, New York Heart Association; PPCM, peripartum cardiomyopathy; RR, respiratory rate; SBP, systemic blood pressure; SO₂, systemic oxygen saturation; SVO₂, systemic (mixed) venous oxygen saturation; WCD, wearable cardioverter defibrillator. Modified from Regitz-Zagrosek et al.⁴

Table 2 Suggested thromboprophylaxis doses for antenatal and postnatal low molecular weight heparin

Weight	Enoxaparin	Dalteparin	Tinzaparin
<50 kg	2000 IU/day	2500 IU/day	3500 IU/day
50–90 kg	4000 IU/day	5000 IU/day	4500 IU/day
91–130 kg	6000 IU/day ^a	7500 IU/day	7000 IU/day ^a
131–170 kg	8000 IU/day ^a	10 000 IU/day	9000 IU/day ^a
>170 kg	60 IU/kg/day ^a	75 IU/kg/day	75 IU/kg/day ^a
High prophylactic dose 50–90 kg	4000 IU b.i.d.	5000 IU b.i.d.	4500 IU/day

From the Royal College of Obstetricians and Gynaecologists, Green-top Guideline 37a (<https://www.rcog.org.uk/globalassets/documents/guidelines/gtg-37a.pdf>).

^aMay be given in two divided doses.

and/or family; the decision for expedite delivery is based on the type and extent of the dissection, haemodynamic instability, gestational age, and evidence of foetal compromise.²⁸

Venous thromboembolic disease

Pregnancy is a risk factor for venous thromboembolic disease. Venous thromboembolism (VTE) during pregnancy is associated with significant morbidity and mortality.^{4,29} Venous thromboembolism risk peaks in the peripartum period, until ~8–12 weeks after delivery.²⁹ Venous thromboembolism risk stratification and the need for prophylactic LMWH therapy are primarily handled by the obstetric care provider. [Supplementary material online, Figure S1](#) summarizes current indications for LMWH prophylaxis during pregnancy; [Table 2](#) lists accepted doses for LMWH prophylaxis during pregnancy. The appropriate VTE prophylaxis strategy for patients with complex CHD (especially women with a Fontan operation) is based on expert opinion and the optimal strategy is still debated.^{4,30}

General cardiologists may be consulted when a pregnant woman presents with suspected clinical VTE (e.g. with signs or symptoms of deep vein thrombosis or pulmonary embolism such as single leg oedema/redness/pain, more often left-sided often with unilateral swelling). The proposed diagnostic algorithm is shown in [Figure 6](#). D-dimer level determination, although clinically used, has limitation because D-dimer increases throughout pregnancy; testing D-dimer is therefore of high negative predictive yet relatively low positive predictive value. Venous ultrasound is particularly useful in ruling out deep venous thrombosis. In a situation of intermediate probability, magnetic resonance venography has been shown to be a reliable diagnostic test before considering chest CT.⁴ Computed tomography pulmonary angiogram should be performed in acutely unwell patients with a high suspicion of pulmonary embolism.

Venous thromboembolism treatment requires therapeutic (weight-adjusted) doses of LMWH.^{4,31} Intravenous infusion of unfractionated heparin (UFH) is often reserved for massive pulmonary embolism, with potential need for additional procedures, such as thrombolysis or embolectomy. Non-vitamin K oral antagonist anticoagulants are not approved during pregnancy. Thrombolytic therapy may be associated with significant risk of placental haemorrhage and foetal mortality (although alteplase does not cross the placenta), and it is usually reserved for severe cases with haemodynamic instability. In these situations, the loading dose of heparin is often withheld and

low-dose infusion heparin drip is started at the end of the thrombolytic drug infusion.⁴

Low molecular weight heparin is then continued for the rest of pregnancy and can, thereafter, be replaced by a vitamin K oral antagonist or a non-vitamin K oral antagonist anticoagulant (depending on breastfeeding).⁴ Anticoagulation management at the time of delivery is summarized at the end of this manuscript. Vitamin K antagonists (VKAs) may be used during breastfeeding and can be started 24–48 h after an uncomplicated delivery, with appropriate bridging with UFH or LMWH. Evidence regarding non-vitamin K oral antagonist anticoagulant use during breastfeeding is lacking; hence, these drugs should not be used if a woman is eager to breastfeed. Long-term anticoagulation should be continued for at least 3 months after pregnancy, or 6 months if the event occurred in the second half of pregnancy, in the absence of other indications for prolonged anticoagulation and risk factors for recurrence.

Prosthetic mechanical heart valves

In women with prosthetic mechanical heart valves (PMHVs), pregnancy-associated cardiovascular complications are common (mWHO Class III).³² Complications include maternal and foetal mortality, maternal thromboembolic events, acute prosthesis dysfunction and haemodynamic instability, potential need for emergency surgery, and maternal/foetal bleeding.³² Vitamin K antagonists are associated with the risk of miscarriage, embryopathy (first trimester exposure), and foetal pathology (including neurological abnormalities) with the risk persisting beyond the first trimester administration.⁴ Recent guidelines suggest two different strategies for managing anticoagulation in women with PMHV based on the average preconception dose of VKA required to achieve the target international normalized ratio (INR) ([Figure 7](#)).^{4,33}

No single strategy is able to simultaneously abolish foetal and maternal risks; therefore, preconception counselling by providers experienced in such practice is essential. Moreover, significant uncertainties exist regarding the appropriate monitoring strategy in women on LMWH, with many authors suggesting that in addition to weekly peak anti-Xa level measurements (with suggested therapeutic target range between 0.8 and 1.2 IU/mL), pre-dose anti-Xa level should be routinely checked to guide LMWH dose (with suggested target level >0.6 IU/mL).^{4,33} The European Society of Cardiology guidelines for the management of cardiovascular disease during pregnancy have expanded the role for VKA administration during

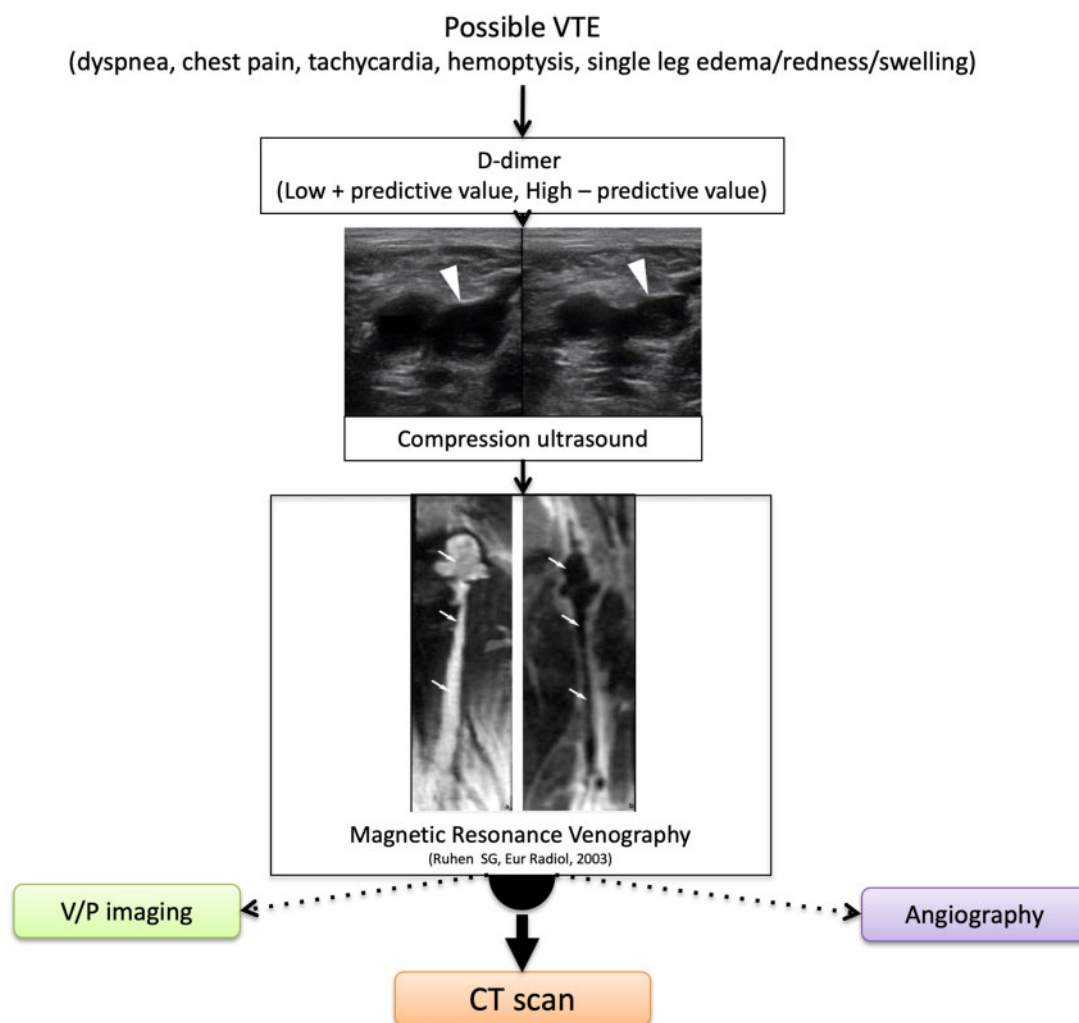


Figure 6 Diagnostic approach for suspected venous thromboembolism during pregnancy. CT, computed tomography; V/P, ventilation–perfusion; VTE, venous thromboembolism.

pregnancy (Figure 7 and Table 3), but there is often resistance by pregnant women and practitioners to consider such a strategy due to the increased risk of foetal complications.

Pregnant women with suspected acute dysfunction of a PMHV or PMHV-related thromboembolic event may present in non-specialist centres. An increase in transvalvular gradient during pregnancy is not diagnostic of valve dysfunction and may be related simply to the increased CO, especially in late pregnancy.

Therefore, clinicians must incorporate clinical status and have high level of suspicion to evaluate patients with advanced imaging such as TOE if necessary. Equivocal cases may be assessed by direct fluoroscopy of the valve using two orthogonal valve projections ('en face' and transversal) to compare opening and closing angles to manufacturer data.³⁴ This investigation requires a low dose of radiation and can be performed safely in pregnancy.

Acute prosthesis dysfunction during pregnancy is a serious, life-threatening event and must be treated as an emergency. Immediate transfer to a tertiary referral centre with expert cardiac surgical

back-up and obstetric support is strongly advised. After achieving full anticoagulation, appropriate management depends on maternal haemodynamic stability, gestational age, foetal health, and surgical risk. Possible strategies include emergency caesarean delivery followed by heart valve surgery if the foetus is viable; or high-risk surgery without interrupting the pregnancy if anticoagulation or other measures fail to restore valve function.⁴ Systemic thrombolysis may be associated with the high risk of systemic embolization (10%), therapy failure, and placental haemorrhage and is usually reserved for very severe valve dysfunction in centres without surgical back-up, or women with prohibitive surgical risk.⁴

Acute coronary syndromes

The exact incidence of coronary artery disease (CAD) in women of child-bearing age is poorly defined.³⁵ Acute coronary syndromes are overall rare (1.7–6.2/100 000 pregnancies) but are responsible for ~20% of cardiovascular mortality during pregnancy.³⁶ The aetiology of CAD in pregnancy may differ from that in the general population,

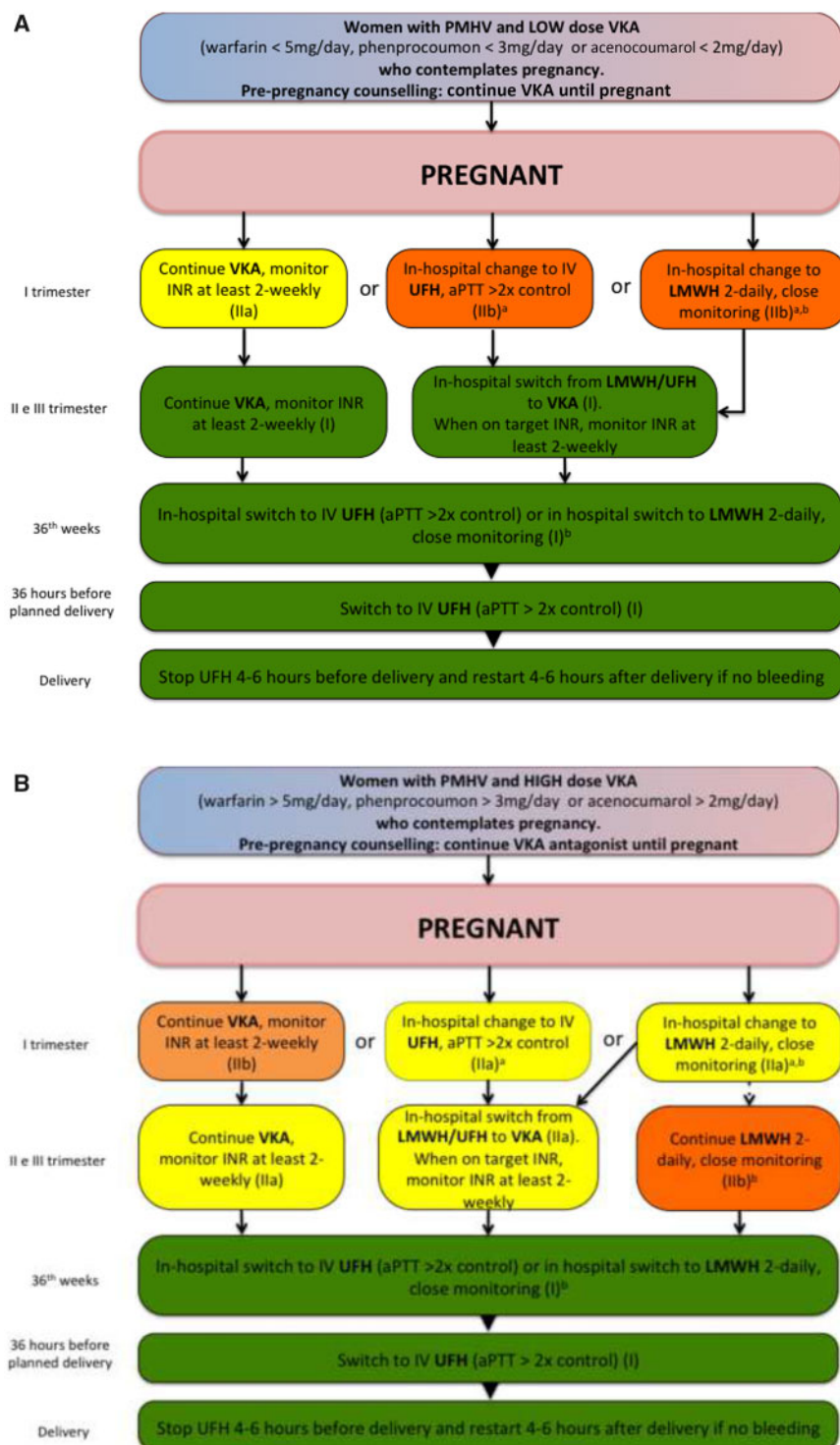


Figure 7 Suggested anticoagulation strategy for women with a prosthetic mechanical heart valve and (A) low-dose preconception vitamin K antagonist or (B) high-dose preconception vitamin K antagonist. (a) Weeks 6–12; (b) monitoring low molecular weight heparin: starting dose for low molecular weight heparin is 1 mg/kg body weight for enoxaparin and 100 IU/kg for dalteparin, twice daily subcutaneously; in-hospital daily anti-Xa levels until target, then weekly (I); target anti-Xa levels: 1.0–1.2 U/mL (mitral and right sided valves) or 0.8–1.2 U/mL (aortic valves) 4–6 h post-dose (I); pre-dose anti-Xa levels >0.6 U/mL (IIb). aPTT, activated partial thromboplastin time; INR, international normalized ratio; i.v., intravenous; LMWH, low molecular weight heparin; PMHV, prosthetic mechanical heart valve; UFH, unfractionated heparin; VKA, vitamin K antagonist. Modified from Regitz-Zagrosek et al.⁴

Table 3 Anticoagulation in mechanical valves and target international normalized ratio for mechanical prostheses

Thrombogenicity of the prosthesis	Number of patient-related risk factors (mitral or tricuspid valve replacement, previous thromboembolism, atrial fibrillation, mitral stenosis any degree, or LVEF <35%)	
	None	≥1
Low (Carbomedics, Medtronic Hall, ATS, Medtronic Open-Pivot, St Jude Medical, On-X, Sorin Bicarbon)	2.5	3.0
Medium (other bileaflet valve with insufficient data)	3.0	3.5
High [Lillehei-Kaster, Omniscience, Starr-Edwards (ball and cage), Bjork-Shiley, other tilting disc valves, any pulmonary valve prosthesis]	3.5	4.0

From Regitz-Zagrosek et al.⁴
LVEF, left (systemic) ventricular ejection fraction.

with increased risk of non-atherosclerotic mechanisms. Spontaneous coronary dissection is a common mechanism of acute coronary event in pregnant women, and it should be always considered in these patients.³⁷ Similarly, myocardial infarction with non-obstructive coronary arteries, and primary coronary thrombosis have been reported.³⁷ The risk of coronary dissection peaks at the end of pregnancy and postpartum; it typically involves the left coronary artery territory, but on occasion may be multi-vessel.³⁷

The general cardiologist should suspect CAD in a pregnant woman with symptoms suggestive of an acute coronary syndrome. During pregnancy, the electrocardiogram often has subtle changes (including non-specific repolarization abnormalities, T-wave inversion) whereas, during anaesthesia-assisted delivery, transient ST-T changes may appear.⁴ High-sensitivity troponin may be helpful for the diagnosis. Differential diagnosis includes pulmonary embolism, aortic dissection, and pre-eclampsia. Acute coronary syndrome during pregnancy may be associated with a rapidly evolving clinical picture and substantial risk of HF, cardiogenic shock, malignant arrhythmias, as well as foetal and maternal mortality.⁴

The management of acute coronary syndromes in pregnancy is similar to the general population. Foetal monitoring and a multidisciplinary approach are essential. Intravenous UFH and oral/sublingual aspirin are safe during pregnancy.⁴ If dual antiplatelet therapy is required, clopidogrel is considered safe during pregnancy but should be maintained for the shortest time.^{4,38} There are very limited safety and efficacy data on bivalirudin, prasugrel, ticagrelor, and glycoprotein IIb/IIIa inhibitors, which are not usually used during pregnancy.³⁸ Beta-blockers are usually advised and safe, although some effects on foetal growth are observed.

The indications for acute revascularization are similar to non-pregnant patients. Periprocedural anticoagulation is associated with increased risk of bleeding, though the risk–benefit ratio supports its use. Ionizing radiation risk should not limit access to revascularization procedures. These are usually performed by experienced operators with limited procedural time and low radiation dose, using abdominal shielding.⁴ Indeed, coronary artery dissection is associated with very fragile coronary arteries and manipulation of intravascular catheters, balloons, and wires can result in the extension of the dissection and

maternal deterioration. Coronary stenting is considered only in case of ongoing symptoms or unstable haemodynamics with flow limiting lesion, new-generation drug-eluting stents are typically advised.^{38,39} Systemic thrombolysis is rarely performed due to limited effectiveness, the high risk of maternal bleeding, and foetal mortality.⁴

Cardiovascular management during delivery and postpartum

The delivery plan and peripartum management does not usually require specific cardiovascular recommendations or support in women with mWHO Class I and II and without significant risk factors. However, some women may be at higher risk at the time of delivery and require careful planning (third trimester multidisciplinary team meeting), deciding on the ideal location where delivery should happen, with early involvement of an experienced anaesthesiology team (Figure 8).⁴ In selected cases with a perceived very high risk of haemodynamic instability (Figure 8), the optimal place for delivery may be a high intensity cardiac environment, where bail-out measures can be implemented rapidly, including surgical intervention or cardiac mechanical circulatory support.

Caesarean delivery does not generally afford protection to pregnant women with cardiovascular disease and is usually associated with increased risk of infection and bleeding; however, it may offer benefits with respect to timing, care coordination and the management of the anticoagulation regimen. Women with high-risk aortopathies and aortic dilatation, symptomatic HF (e.g. severe left/systemic ventricular dysfunction), symptomatic aortic stenosis, refractory arrhythmias with haemodynamic instability, or pulmonary arterial hypertension may benefit from the faster delivery offered by caesarean section but many of these women can also deliver safely via vaginal birth in the proper setting. Caesarean delivery is recommended for the fully anticoagulated woman who presents in labour,

	Standard profile	Cardiac red flags for C-section	Very high risk delivery
			
 Functional class	NYHA I-II	NYHA III-IV	NYHA III-IV
 Myocardial dysfunction	Absent	Present and severe	Severe with symptoms
 Aorta and connective tissue disorder	▶ Normal aorta (including bicuspid aortic valve) ▶ Mildly dilated aorta ▶ Low risk connective tissue disorder ▶ Lesion- and disease-specific threshold apply	▶ Significant (and progressive) aortic dilation ▶ High risk connective tissue disorders ▶ Expert advice is required ▶ Lesion- and disease-specific threshold apply	▶ Severe aortic dilation with pregnancy-induced rapid growing ▶ Acute aortic syndromes ▶ Women with indication to prophylactic aortic surgery
 Valvular heart disease	▶ No valvular heart disease ▶ Mild or moderate heart valve disease ▶ Biologic prosthetic heart valve (including homograft, autograft or tissue-engineered surgical conduit) without severe dysfunction	▶ Mechanical heart valve ▶ Severe and symptomatic aortic or severe mitral valve disease	▶ Acute mechanical heart valve dysfunction ▶ Symptomatic and severe mitral valve stenosis ▶ Severe aortic stenosis with severe LV systolic dysfunction
 Pulmonary arterial hypertension	Absent	Present	Present with severe and symptomatic RV failure

Figure 8 Cardiac care at the time of delivery. Clinical factors and 'red flags' for cardiovascular indication to caesarean delivery are presented along with clinical profiles associated with very high risk of cardiovascular complications at the time of delivery. In this latest group of patients, individualized expert decision may consider location of delivery in a high-intensity cardiac environment with rapid access to surgical back-up including mechanical circulatory support or extracorporeal membrane oxygenation program. ECMO, extracorporeal membrane oxygenation; LV, left ventricle; NYHA, New York Heart Association; RV, right ventricle.

primarily due to concerns of foetal bleeding during vaginal delivery.⁴

Maternal monitoring during labour in women with heart disease often consists of continuous electrocardiogram (ECG) monitoring, oxygen saturation control, and non-invasive blood pressure measurement. Invasive arterial pressure monitoring or central venous catheterization is rarely indicated and discussed on a case-by-case basis during the third trimester in a multidisciplinary setting, when formulating an individualized delivery plan.^{4,40,41} Pulmonary artery (PA) catheter placement is not standard practice, with the added potential risk of vascular lesions, including PA dissection, in particular in patients with pulmonary arterial hypertension.⁴

Anticoagulation, antiplatelet therapy, and bleeding complications during pregnancy

Prophylactic and therapeutic anticoagulation is often required during pregnancy for cardiac and non-cardiac reasons.⁴² As previously discussed, weight-based UFH and LMWH are consolidated strategies for the majority of clinical scenarios, except for women with a mechanical heart valve. While strict anti-Xa level dosing may not be required in many patients, less strict anti-Xa dosing may be reasonable in patients with large weight fluctuation.

Anticoagulation in women with mechanical heart valves does, however, require a different approach. In these women, strict anti-Xa level is required if LMWH administration is considered, even though the risk of thrombotic complications remains higher than with vitamin K oral antagonists.⁴ However, patient and physician reluctance to accept the risk of drug-induced embryopathy or foetal abnormalities means that vitamin K oral antagonists are often discontinued and replaced by heparin, at least for the first trimester.⁴²

A particularly challenging scenario is heparin-induced thrombocytopenia (HIT) in a pregnant woman on therapeutic anticoagulation.⁴³ The diagnosis of HIT requires immediate cessation of UFH or LMWH and early institution of an alternative anticoagulation strategy.⁴³ Common approaches include fondaparinux (a synthetic pentasaccharide, which does not cross-react with HIT antibodies and has little placental transfer), bivalirudin or argatroban. For the latter two, there may be placental crossing, hence are less often used.⁴³

Labour, delivery, and postpartum are challenging in women on therapeutic anticoagulation. After week 36 of gestation, anticoagulation is achieved either by twice daily subcutaneous LMWH or intravenous continuous UFH infusion (in hospital), depending on the maternal thromboembolic risk profile (Figure 7). Low molecular weight heparin should be withheld the day/night prior to induction, or at least 24 h before delivery or epidural catheter placement. In women on heparin infusion, this may be discontinued 6 h before the expected time of delivery or epidural catheter placement. In women at very high risk for thromboembolic complication (such as PMHV), the timing of restoration of full anticoagulation may be 6 h after vaginal delivery and 12 h after caesarean delivery, depending on the haemostasis and bleeding risk.⁴

Unplanned active labour and delivery in a woman on full anticoagulation carries very high risks of maternal and neonatal complications.

Unfractionated heparin can be successfully reversed with protamine (dose depending upon heparin dose, see <https://www.medicines.org.uk/emc/> for details).⁴ Low molecular weight heparin reversal is less predictable and repeated protamine may be necessary to control the bleeding.

Labour and delivery in women on VKAs carry particularly high risks. Caesarean delivery is generally recommended to reduce foetal/neonatal bleeding complications during the second stage of labour.⁴ Prothrombin complex is often administered with dose adjustment on maternal weight and INR. This strategy is usually preferred over frozen fresh plasma administration (10–15 mL/kg). Caesarean delivery should ideally be performed with an INR <1.5. Vitamin K is usually administered (except in women with a prosthetic heart valve), but its effect on the coagulation profile is delayed (between 8 and 12 h from administration) and, thus, its clinical utility may be limited. The neonate may present significant and prolonged anticoagulation (up to 8–10 h) requiring fresh frozen plasma in addition to routine intramuscular vitamin K.

Low-dose aspirin is safe during pregnancy.⁴ Clopidogrel is considered reasonable for the minimum possible time for which it is clinically indicated, but ticagrelor, prasugrel, or glycoprotein IIb/IIIa inhibitors are avoided during pregnancy.⁴

Conclusion

Cardiovascular complications during pregnancy are important causes of maternal, obstetric, and foetal morbidity and mortality. Care should be provided in centres with an established multidisciplinary pregnancy and heart disease team. General cardiologists and emergency physicians may encounter such patients in an emergency or acute setting; vigilance is required to identify the diagnosis and complications, seeking prompt advice and support from tertiary referral centres to initiate appropriate treatment and transfer the patient when safe.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

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