
IRAQ: INSIDE THE OCCUPATION / THE SEARCH FOR SADDAM
TIME
WOMEN & HEART DISEASE
Is your biggest worry breast cancer? Think again. ONE OUT OF THREE women will die of heart disease. What you can do to protect yourself

Population of Europe of Childbearing Age

EU population 2008
499 million total*

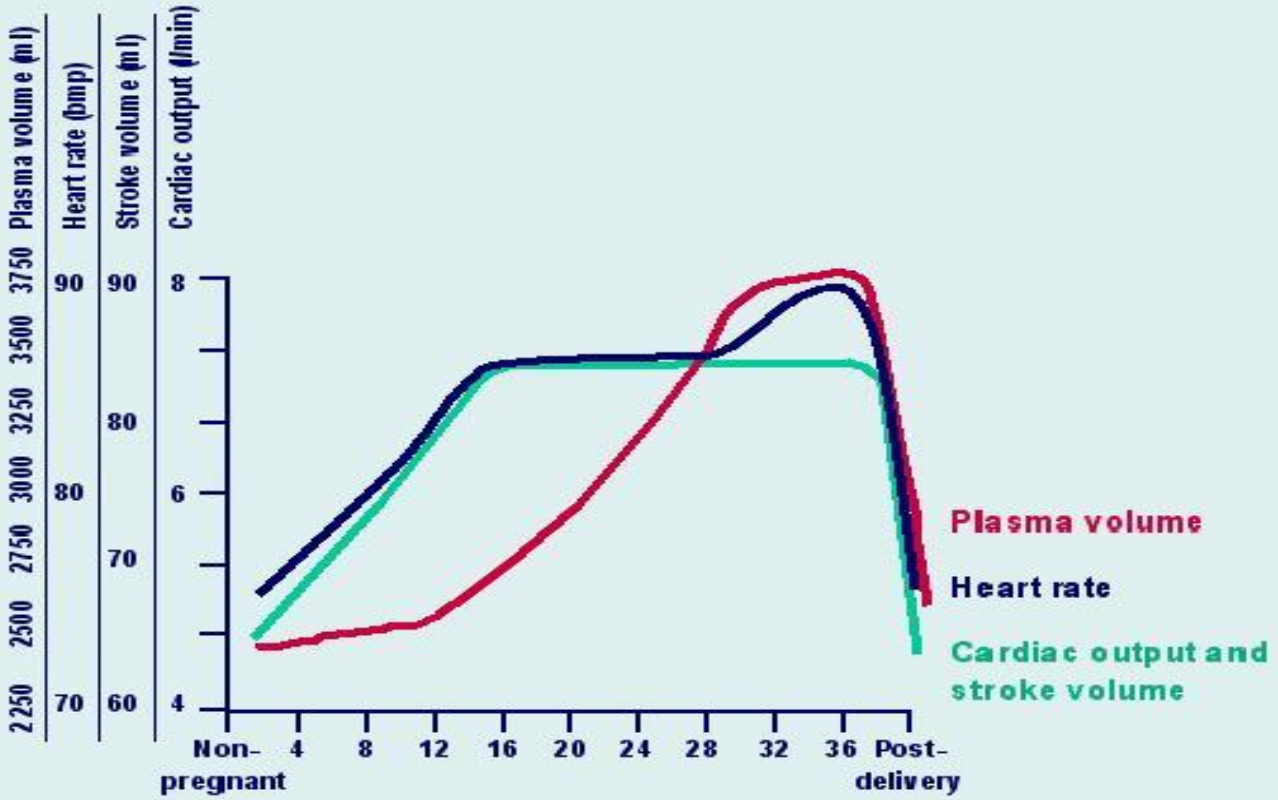
- 105 million women in childbearing age (15-45 years).
- 5 million live births.
- 1% of pregnancies are complicated by heart disease.**

*http://epp.eurostat.ec.europa.eu/portal/page/portal/population/data
**Report on Maternal Deaths in UK RCOG

2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy
European Heart Journal (2018) 00, 1–83- doi:10.1093/eurheartj/ehy 340

Haemodynamic Changes During Pregnancy

- ↑ blood volume ≈ 50%.
- ↑ cardiac output 30-50% maximum between, 5th and 8th months.
- ↓ systolic and diastolic blood pressure.
- ↓ systemic arterial resistance (hormones, placenta).



Thorne Heart 2004;90:450-6

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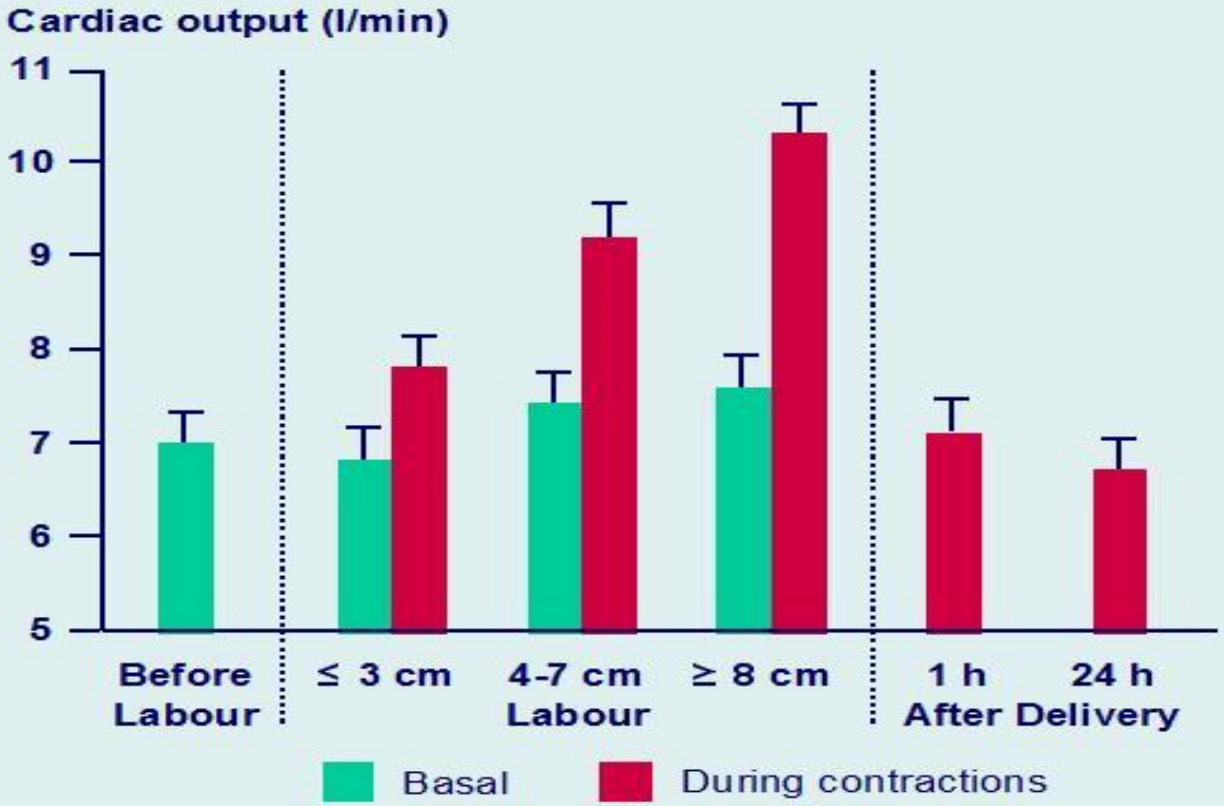
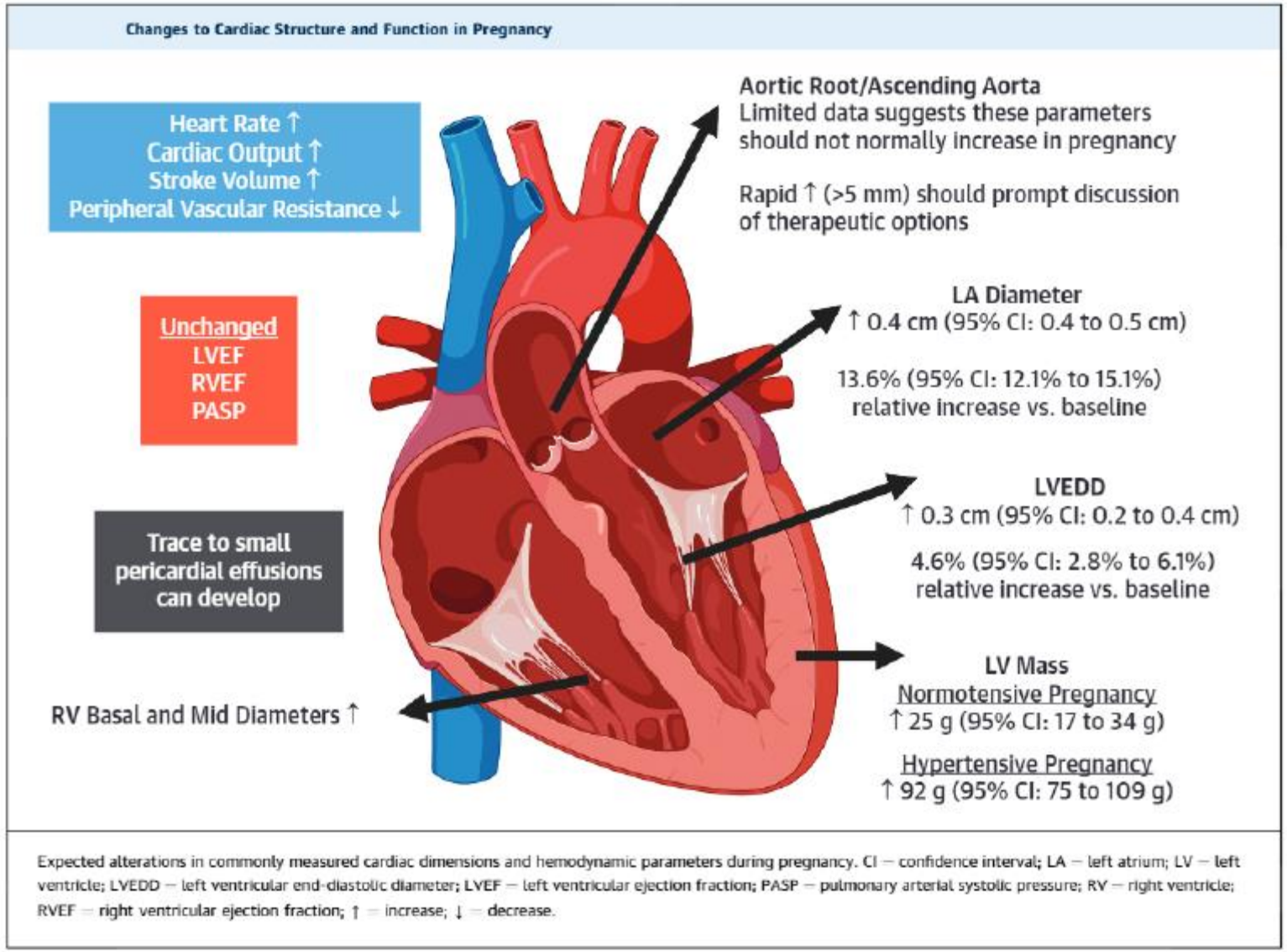
Haemodynamic Changes During Delivery

- Labour:
  - ↑ O_2 consumption,
  - ↑ baseline cardiac output,
  - ↑ cardiac output and blood pressure during uterine contractions, depending on modalities of delivery (epidural analgesia, Cesarean section)
- Post-partum:
  - ↑ blood shift from placenta,
  - ↑ preload and cardiac output.



Hunter et al. *Br Med J* 1992;68:540-3



Expected alterations in commonly measured cardiac dimensions and hemodynamic parameters during pregnancy. CI = confidence interval; LA = left atrium; LV = left ventricle; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; PASP = pulmonary arterial systolic pressure; RV = right ventricle; RVEF = right ventricular ejection fraction; ↑ = increase; ↓ = decrease.

Nataly Bello et al. *J Am Coll Cardiol* 2021; 77:1813-1822

Other Changes during Pregnancy

- Haemostasis:
  - increased platelet adhesiveness,
  - increased concentration of coagulation factors, fibrinogen,
  - impaired fibrinolysis.

    → ***Hypercoagulability***
- Maternal glucose metabolism.
- Drug metabolism:
  - absorption, excretion, and bioavailability.

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Pre-pregnancy

ESC European Society of Cardiology

Indications for intervention (surgical or catheter) do not differ in women who consider pregnancy compared with other patients. There are a few exceptions, such as **severe aortic dilatation** and **severe asymptomatic mitral stenosis**.

Recommendations	Class	Level
Pre-pregnancy risk assessment and counselling is indicated in all women with known or suspected congenital or acquired cardiovascular and aortic disease.	I	C
It is recommended to perform risk assessment in all women with cardiac diseases of childbearing age and after conception, using the **mWHO** classification of maternal risk.	I	C
It is recommended that high-risk patients are treated in specialized centres by a multidisciplinary **pregnancy heart team**.	I	C
It is recommended that the valve prosthesis for a woman contemplating pregnancy is chosen in consultation with a pregnancy heart team.	I	C

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doi:10.109

Pre-pregnancy counseling

- Maternal risk of complications during pregnancy
- Possible irreversible effects of pregnancy on the maternal cardiac condition
- Fetal risk (miscarriage, birth weight, small for gestational age)
- Medication use
- Genetic aspects
- Longterm prognosis of the mother

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The Cardio-Obstetrics Model of Care

- Cardio-obstetrics involves clinicians from multiple specialties focused on pregnant patients from preconception through the postpartum period.
- Risk assessment tools can guide conversations about maternal and fetal risks in women with cardiovascular disease who are pregnant or considering pregnancy.
- The cardio-obstetrics team should anticipate potential cardiovascular complications of pregnancy, labor and delivery, and the postpartum period.
- Postpartum care is an ongoing, integral component of cardio-obstetrical patient managemen

ΕΙΔΙΚΗ ΟΜΑΔΑ ΚΥΗΣΗΣ

mWHO II-III
mWHO III
mWHO IV

Πνευμονολόγος

Γενετιστής

Καρδιολόγος

Καρδιοχειρουργός

Μαιευτήρας

Εξειδικευμένη νοσηλεύτρια

Παιδοκαρδιολόγος

Εξειδικευμένη μαία

Αναισθησιολόγος

Νεογνολόγος

Αιματολόγος

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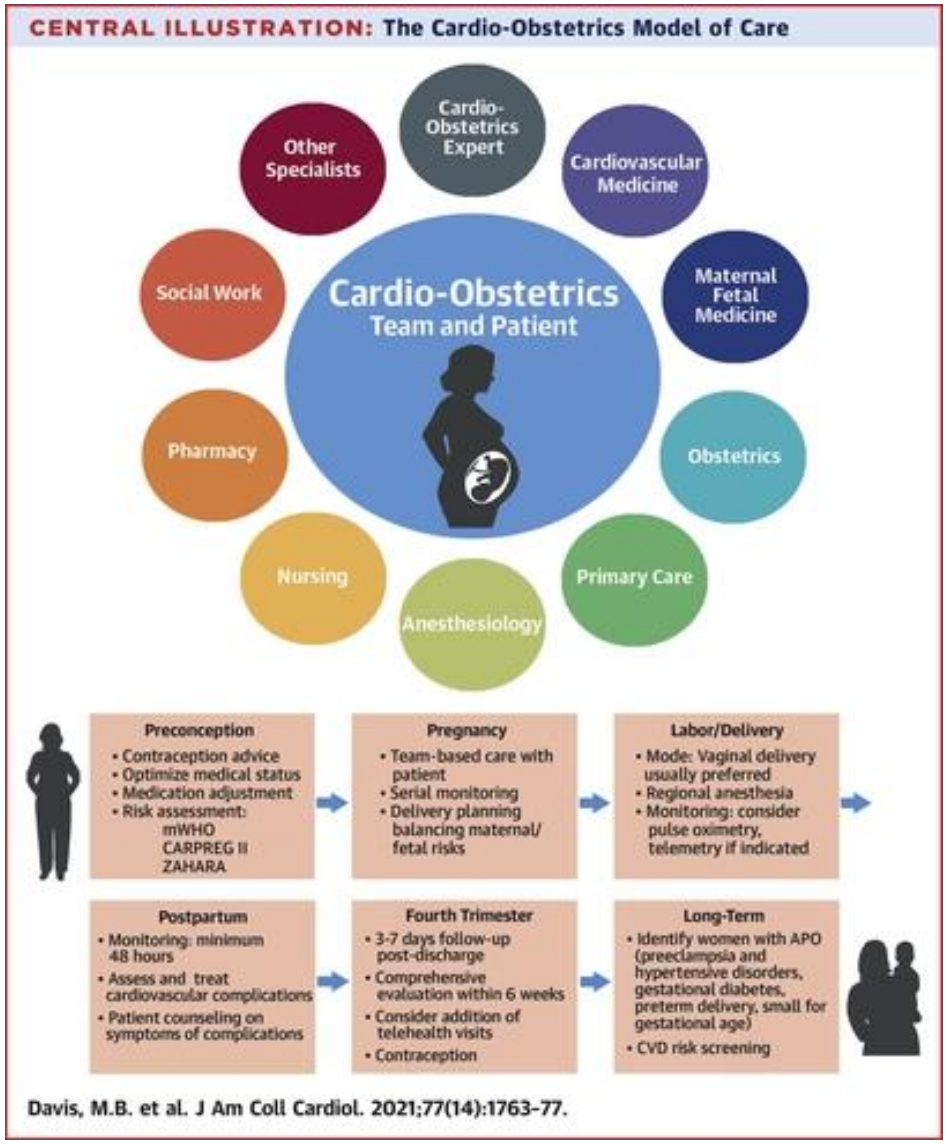
The Cardio-Obstetrics Model of Care



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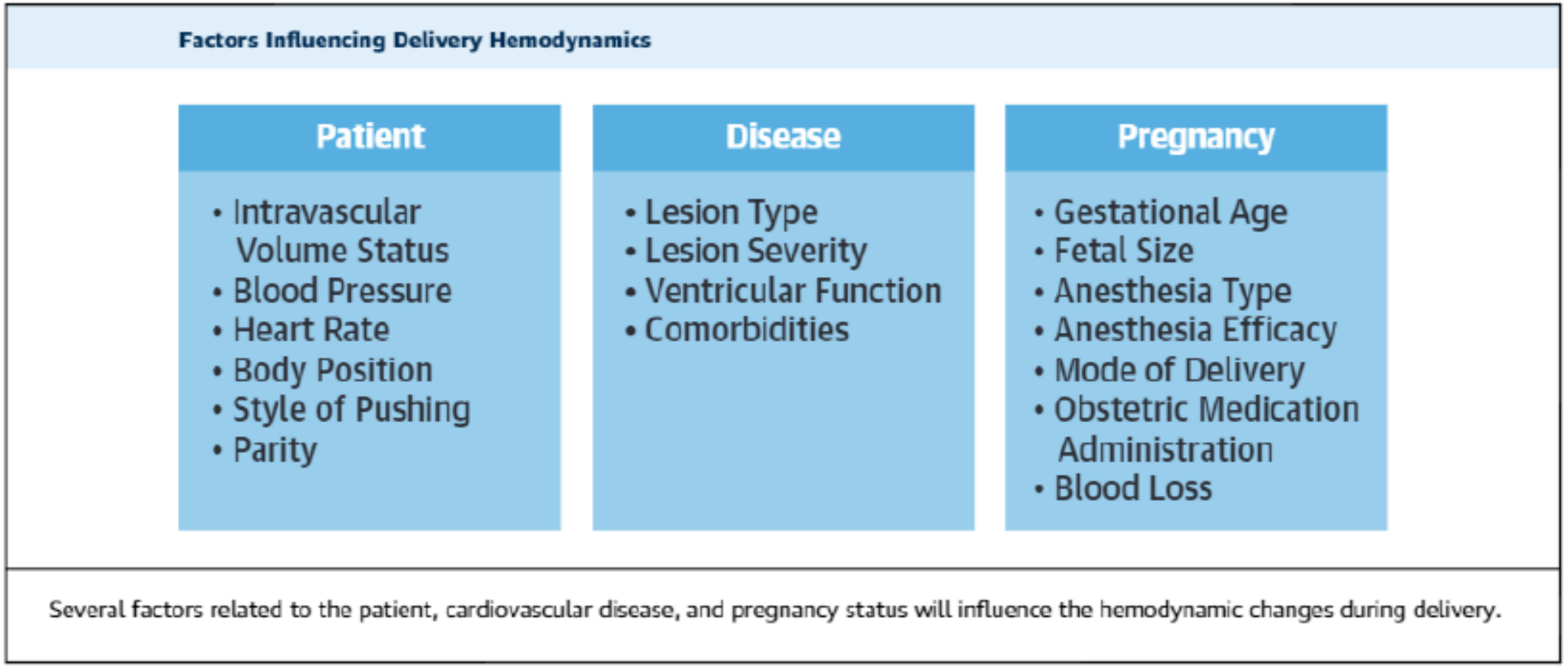
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Melinda B. Davis et al. *J Am Coll Cardiol* 2021; 77:1763-1777



Melinda B. Davis et al. *J Am Coll Cardiol* 2021; 77:1763-1777

Cardiovascular Diagnosis

- Clinical assessment: diagno
  - case history,
  - examination: auscultation
- ECG.
- Echocardiography.
- Magnetic resonance imagi
  - without gadolinium.
- Exercise testing:
  - before pregnancy,
  - during pregnancy (80% c

In most pregnant patients, the heart rotates to the left with a 15–20° leftward axis deviation on the ECG. Common additional findings include transient ST/T wave changes, a Q wave and inverted T waves in lead III, an attenuated Q wave in lead aVF, and inverted T waves in V1, V2, and occasionally V3. Changes may mimic LV hypertrophy and other structural heart diseases.

Transthoracic echocardiography is the preferred imaging method

Physiological congenital heart disease and valve disease, and sexercise testing is an integral part of follow-up in adult hould be performed in patients with known heart disease who plan pregnancy. This Task Force recommends submaximal exercise testing (80% of predicted maximal heart rate) in asymptomatic patients with suspected heart disease if already pregnant. There is no evidence that it increases the risk of spontaneous miscarriage.[30] Stress echocardiography using bicycle ergometry may improve diagnostic specificity.Dobutamine stress is rarely indicated during pregnancy and, because pregnancy in itself is a stress test, its use should be avoided when other options are available.

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2018 ESC Guideline
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Cardiovascular Diagnosis

- Clinical ass
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- ECG.
- Echocardio
- Magnetic re
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Εξέταση	Σχόλια
Ηλεκτροκαρδιογράφημα	Συστήνεται σε όλες τις περιπτώσεις.
Υπερηχογράφημα καρδιάς	Συστήνεται σε κάθε έγκυο που έχει ανεξήγητα ή πρωτοεμφανιζόμενα σημεία και συμπτώματα καρδιαγγειακής νόσου. Σε αορτοπάθειες προτείνεται συχνότερος έλεγχος ανάλογα με την αρχική διάμετρο της αορτής.
Νατριουρητικά πεπτίδια	Σε περίπτωση νέων συμπτωμάτων ή σημείων που σχετίζονται με καρδιακή ανεπάρκεια. Σε γνωστό ιστορικό καρδιαγγειακής νόσου είναι καλό να υπάρχει μια αρχική τιμή αναφοράς
Holter ρυθμού	Σε αίσθημα παλμών ή ανεξήγητα επεισόδια συγκοπής.
Δοκιμασία κόπωσης	Σε γυναίκες με γνωστή καρδιακή νόσο που επιθυμούν κύηση. Κατά την εγκυμοσύνη υπομέγιστη δοκιμασία (80% της προβλεπόμενης καρδιακής συχνότητας) σε ασυμπτωματικές γυναίκες που υποψιαζόμαστε καρδιοπάθεια.
Μαγνητική τομογραφία καρδιάς	Όταν δεν είναι ξεκάθαρη η διάγνωση προτιμάται από απεικονιστικές μεθόδους που χρησιμοποιούν ιονίζουσα ακτινοβολία. Θα πρέπει να αποφεύγεται η έγχυση γαδολινίου.
Αξονική τομογραφία	Αντενδείκνυται στη κύηση εκτός εάν άλλες διαγνωστικές μέθοδοι δεν είναι επαρκείς, όπως πχ στη διάγνωση ή αποκλεισμό πνευμονικής εμβολής ή οξέος αορτικού συνδρόμου. Στις περιπτώσεις αυτές χρησιμοποιείται το πρωτόκολλο με χαμηλή ακτινοβολία.
Καρδιακός καθετηριασμός	Σπάνια για διαγνωστικούς λόγους στην κύηση.

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Cardiovascular Diagnosis

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Τροποποίηση παραγόντων κινδύνου	• Διακοπή καπνίσματος • Διακοπή κατανάλωσης αλκοόλ • Αντιμετώπιση συννοσηρότητων (αρτηριακής υπέρτασης, διαβήτη, παχυσαρκίας) • Φυσική δραστηριότητα
Επεμβατική αντιμετώπιση βαλβιδοπαθειών/ συγγενών καρδιοπαθειών πριν την κύηση	• Σημαντική **στένωση μιτροειδούς βαλβίδας** με στόμιο<1.5cm^2 • Σοβαρή **στένωση αορτικής βαλβίδας** με παρουσία συμπτωμάτων ή με έκπτωση της λειτουργικότητας της αριστερής κοιλίας (κλάσμα εξώθησης<50%) ή με εμφάνιση συμπτωματολογίας κατά την δοκιμασία κόπωσης ή πτώση πίεσης κατά τη διάρκεια αυτής • Σοβαρή **ανεπάρκεια αορτικής ή μιτροειδούς βαλβίδας** και παρουσία συμπτωμάτων, έκπτωση της λειτουργικότητας ή διάταση της αριστερής κοιλίας • Αιμοδυναμικά σημαντικές βλάβες (π.χ. στένωση ισθμού αορτής, στένωση πνευμονικής βαλβίδας και κλάδων, κ.α.) σε συγγενείς καρδιοπάθειες
Έλεγχος για πιθανή τροποποίηση της λαμβανόμενης φαρμακευτικής αγωγής (συμπεριλαμβανομένης της αντιπηκτικής)	

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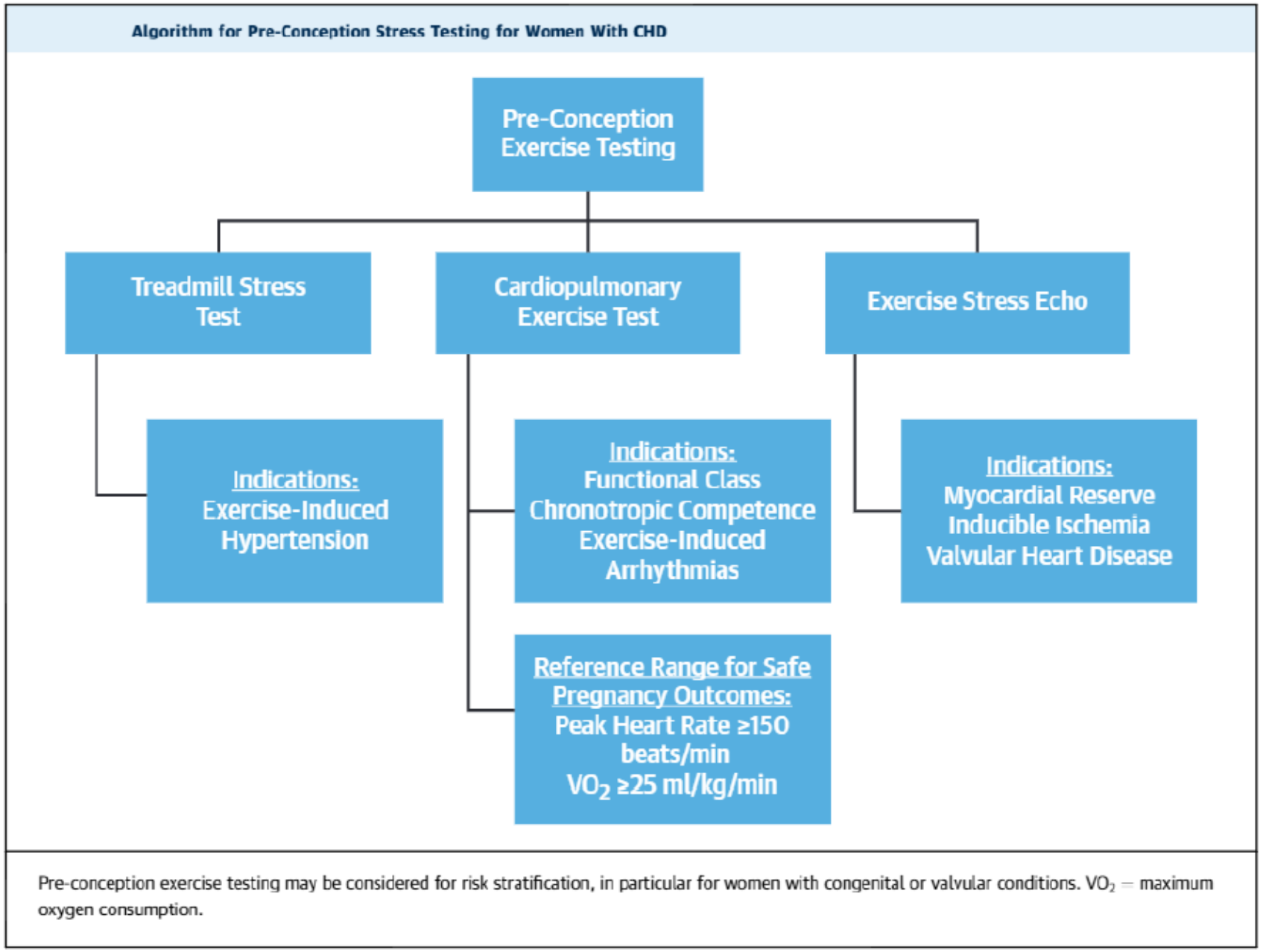


Pre-conception exercise testing may be considered for risk stratification, in particular for women with congenital or valvular conditions. VO_2 = maximum oxygen consumption.

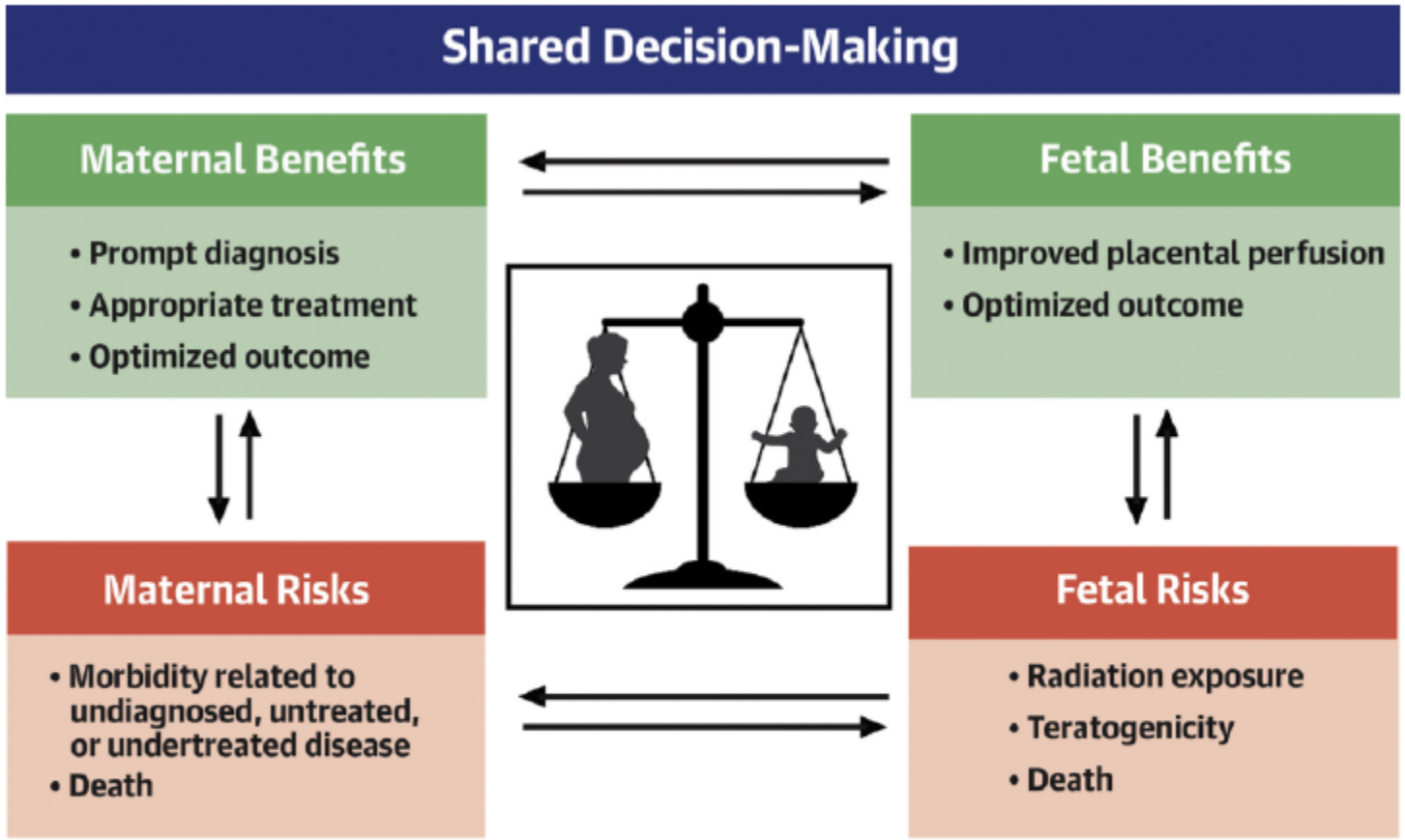
Kathryn J. Lindley et al. *J Am Coll Cardiol* 2021; 77:1778-1798

Radiation Exposure

- No evidence of increased fetal risk for doses < 50 mGy.
- Avoid radiation exposure, in particular before 12 weeks.
- Main exceptions:
  - CT scan for pulmonary embolism,
  - percutaneous cardiac interventions.

Procedure	Fetal exposure		Maternal exposure	
Chest radiograph (PA and lateral)	< 0.01 mGy	< 0.01 mSv	0.1 mGy	0.1 mSv
CT chest	0.3 mGy	0.3 mSv	7 mGy	7 mSv
Coronorary angiography	1.5 mGy	1.5 mSv	7 mGy	7 mSv
PCI or radiofrequency catheter ablation	3 mGy	3 mSv	15 mGy	15 mSv

CENTRAL ILLUSTRATION Shared Decision-Making Is the Cornerstone of Providing Optimal Care to Pregnant Women



Bello, N.A. et al. J Am Coll Cardiol. 2021;77(14):1813-22.

When choosing diagnostic tests and medications for pregnant and lactating women, the interplay between maternal and fetal/infant risks and benefits must be carefully considered. Shared decision-making in consultation with the patient and cardio-obstetrics team is essential for optimal outcomes.

Nataly Bello et al. *J Am Coll Cardiol* 2021; 77:1813-1822

Summary of Possible In Utero Induced Deterministic Radiation Effects by Gestational Age and Radiation Dosage

Gestational Age (Weeks)	<50 mGy	50–100 mGy	>100 mGy
0 to 2	None	None	None
3 to 4	None	Probably none	Possible spontaneous abortion
5 to 10	None	Scientifically uncertain and probably too subtle to be clinically detectable	Possible malformation risk increases with increasing dose
11 to 17	None	Scientifically uncertain and probably too subtle to be clinically detectable	Risk of diminished IQ increases with increasing dose
18 to 27	None	None	IQ deficits not detectable at diagnostic doses
>27	None	None	None applicable to diagnostic medicine

IQ = intelligence quotient.

Average Radiation Exposure From Common Cardiac Imaging Procedures

Imaging Modality	Fetal Dose (mGy)
Ultrasound	0
MRI	0
CXR	0.002–0.1
CT chest or CT pulmonary angiography	0.03–0.66
V/Q scan	0.32–0.74
Low-dose perfusion scintigraphy	0.1–0.5
Fluoroscopy (diagnostic/therapeutic angiography, balloon valvuloplasty)	3–20
PET CT	10–50

CT = computed tomography; CXR = chest x-ray; MRI = magnetic resonance imaging; PET = positron emission tomography; V/Q = ventilation/perfusion.

Nataly Bello et al. *J Am Coll Cardiol* 2021; 77:1813-1822

Timing and Mode of Delivery

- Favour spontaneous onset of labour and vaginal delivery in most cases of stable heart disease.
- Wide use of lumbar epidural analgesia.
- Indications for Caesarean section:
  - pre-term labour in patients on oral anticoagulants,
  - Marfan and other ascending aortic aneurysms (IIaC if > 45 mm, IIbC if 40-45 mm),
  - aortic dissection (IIaC),
  - severe aortic stenosis (IIaC),
  - Eisenmenger syndrome (IIaC).
- Multidisciplinary care for high-risk patients.

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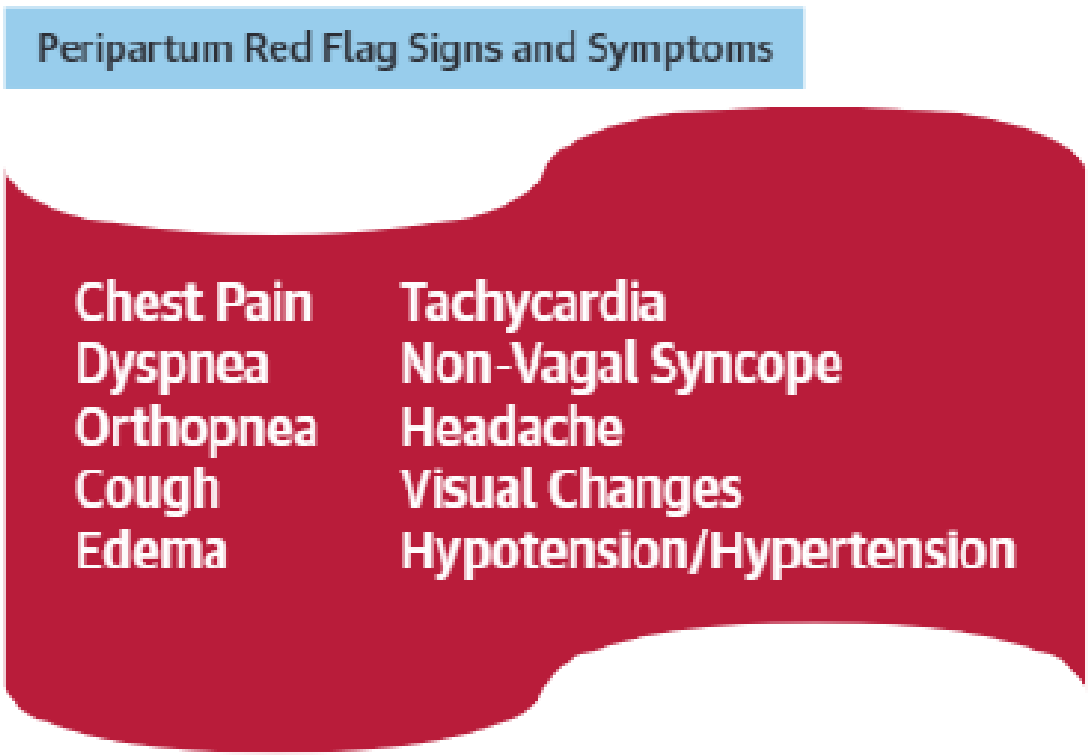
FIGURE 3 Signs and Symptoms Concerning for Cardiovascular Complications During or After Pregnancy



Patients and clinicians need to be aware of signs and symptoms that may signal cardiovascular complications during and after pregnancy.

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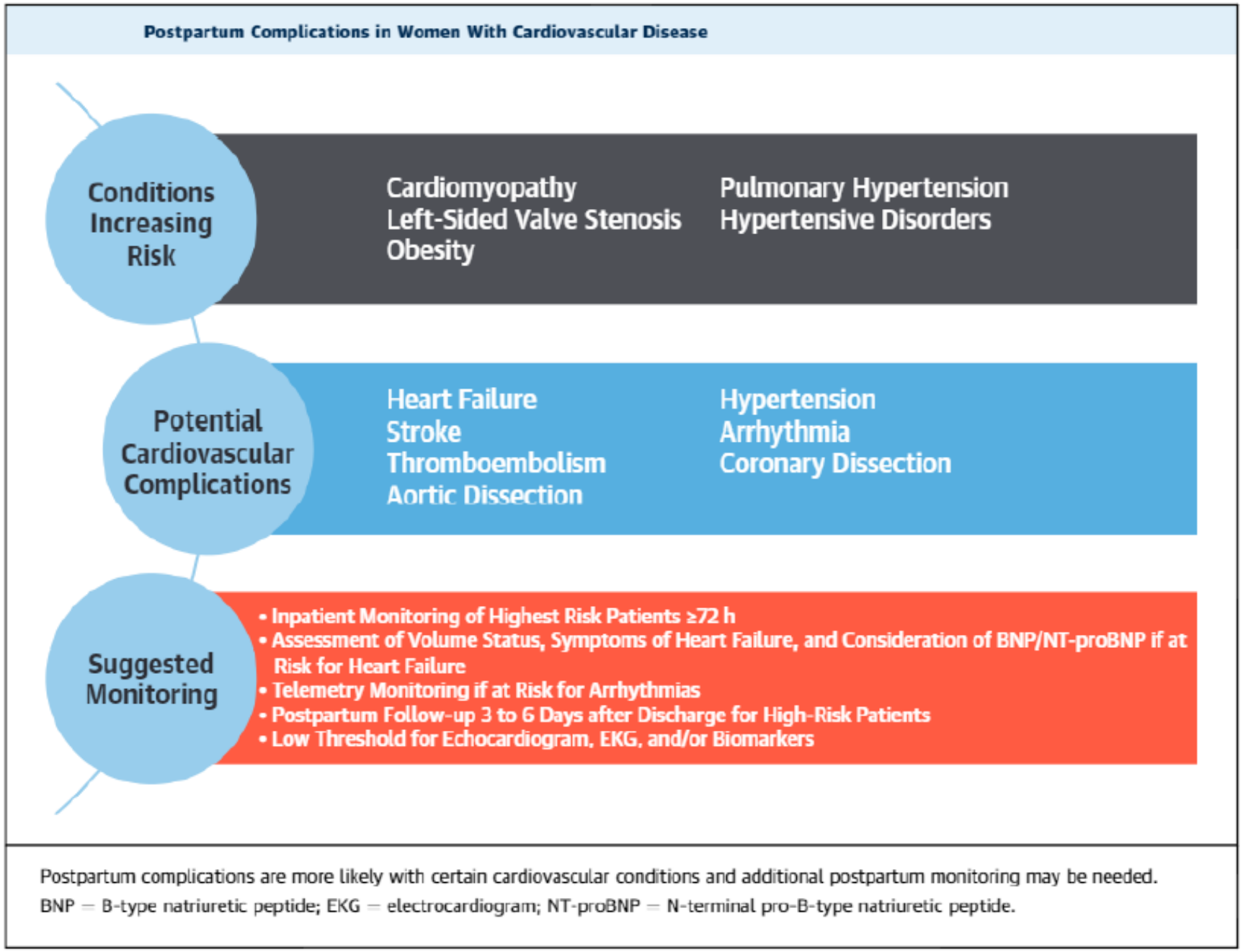
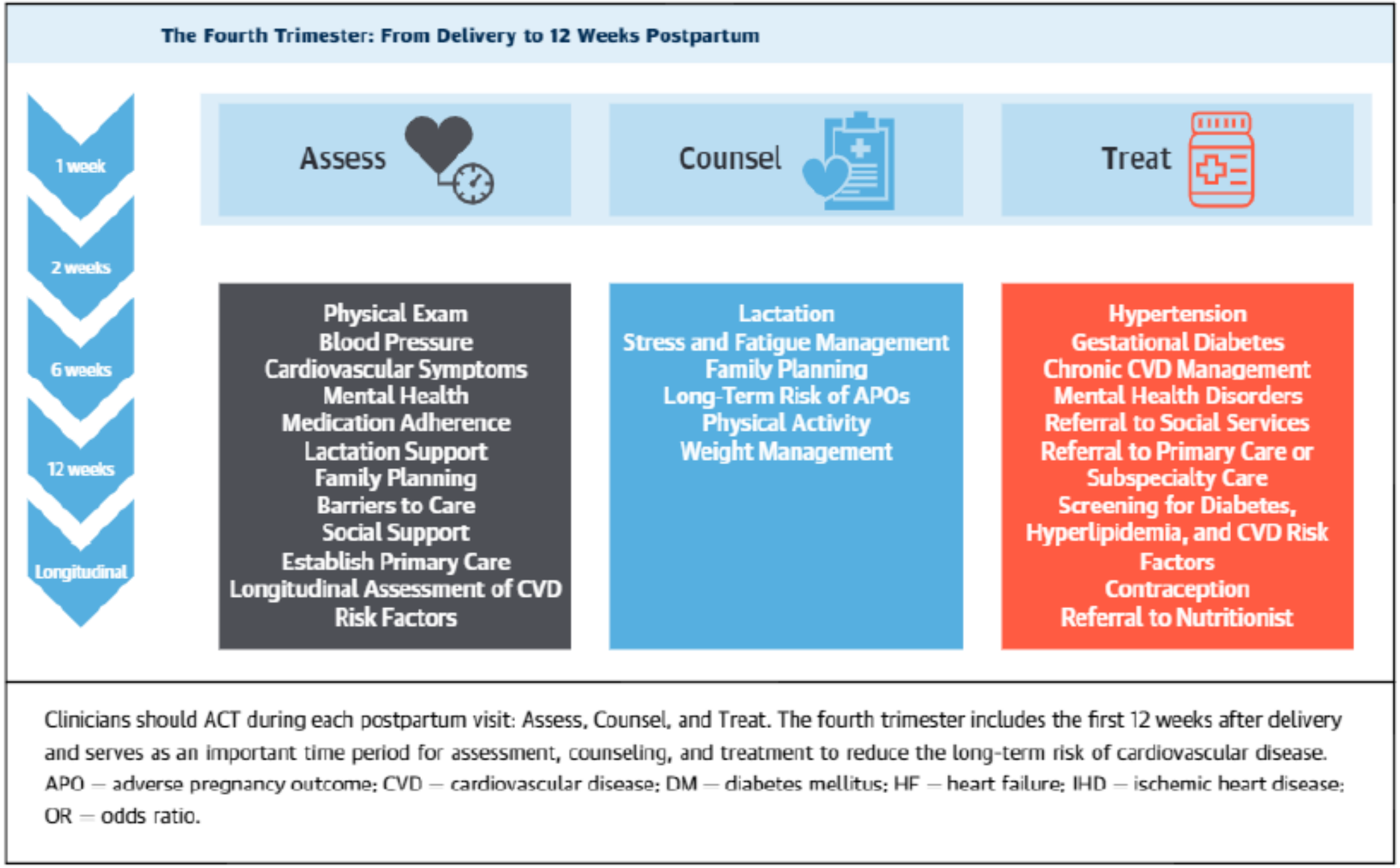


Postpartum complications are more likely with certain cardiovascular conditions and additional postpartum monitoring may be needed.
BNP = B-type natriuretic peptide; EKG = electrocardiogram; NT-proBNP = N-terminal pro-B-type natriuretic peptide.

Melinda B. Davis et al. *J Am Coll Cardiol* 2021; 77:1763-1777



Clinicians should ACT during each postpartum visit: Assess, Counsel, and Treat. The fourth trimester includes the first 12 weeks after delivery and serves as an important time period for assessment, counseling, and treatment to reduce the long-term risk of cardiovascular disease. APO = adverse pregnancy outcome; CVD = cardiovascular disease; DM = diabetes mellitus; HF = heart failure; IHD = ischemic heart disease; OR = odds ratio.

Melinda B. Davis et al. *J Am Coll Cardiol* 2021; 77:1763-1777

Risk assessment by mWHO classification

	mWHO I	mWHO II	mWHO II–III	mWHO III	mWHO IV
Diagnosis (if otherwise well and uncomplicated)	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 ectopic beats, isolated	Unoperated atrial or ventricular septal defect Repaired tetralogy of Fallot Most arrhythmias (supraventricular arrhythmias) Turner syndrome without aortic dilatation	Mild left ventricular impairment (EF > 45%) HCM Native or tissue valve disease not considered WHO I or IV (mild MS, moderate AS) Marfan or other HTAD syndrome without aortic dilatation Aorta < 45 mm in bicuspid aortic valve pathology Repaired coarctation Atrioventricular septal defect	Moderate LV impairment Previous PPCM without residual left ventricular impairment Mechanical valve Systemic RV 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 MS Severe asymptomatic AS Moderate aortic dilatation VT	Pulmonary arterial hypertension Severe systemic ventricular dysfunction (EF < 30% or NYHA class III–IV) Previous peripartum cardiomyopathy with any residual left ventricular impairment Severe MS Severe symptomatic AS Systemic right ventricle with moderate or severely decreased ventricular function Severe aortic dilatation Vascular Ehlers–Danlos Severe coarctation Fontan with complic.

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European Heart Journal (2018) 00, 1–83- doi:10.1093/eurheartj/ehy 340

Risk assessment by mWHO classification

	mWHO I	mWHO II	mWHO II–III	mWHO III	mWHO IV
Risk	No detectable increased risk of maternal mortality and no/mild increased risk in morbidity	Small increased risk of maternal mortality or moderate increase in morbidity	Intermediate increased risk of maternal mortality or moderate to severe increase in morbidity	Significantly increased risk of maternal mortality or severe morbidity	Extremely high risk of maternal mortality or severe morbidity
Maternal cardiac event	2.5–5%	5.7–10.5%	10–19%	19–27%	40–100%
Counselling	Yes	Yes	Yes	Yes: expert counselling required	Yes: pregnancy contra-indicated. If pregnancy occurs discuss termination
Care during pregnancy	Local hospital	Local hospital	Referral hospital	Expert centre for pregnancy and cardiac disease	Expert centre for pregnancy and cardiac disease
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

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Risk assessment by mWHO classification

	mWHO I	mWHO II	mWHO II-III	mWHO III	mWHO IV
Διάγνωση	• Ήπια -στένωση πνευμονικής βαλβίδας -ανοιχτός βοτάλειος πόρος -πρόπτωση μιτροειδούς βαλβίδας • Επιτυχώς διορθωμένες απλές ανωμαλίες -μεσοκολπική επικοινωνία -μεσοκοιλιακή επικοινωνία -ανοιχτός βοτάλειος πόρος -ανώμαλη εκβολή πνευμονικών φλεβών • Μεμονωμένες, έκτακτες κολπικές ή κοιλιακές συστολές	• Μη χειρουργηθείσα μεσοκολπική/ μεσοκοιλιακή επικοινωνία • Διορθωμένη τετραλογία Fallot • Πλειονότητα των αρρυθμιών (υπερκοιλιακές αρρυθμίες) • Σύνδρομο Turner χωρίς διάταση της αορτής	• Ήπια έκπτωση της λειτουργικότητας της αριστερής κοιλίας (ΚΕ >45%) • Υπερτροφική μυοκαρδιοπάθεια • Βαλβιδοπάθειες που δεν ανήκουν σε WHOI ή IV (ήπια στένωση μιτροειδούς βαλβίδας, μέτρια στένωση αορτικής βαλβίδας) • Σύνδρομο Marfan ή άλλη κληρονομική θωρακική αορτοπάθεια χωρίς διάταση της αορτής • Αορτή < 45mm σε αορτοπάθειες σχετιζόμενες με δίπτυχη αορτική βαλβίδα • Διορθωμένη στένωση του ισθμού της αορτής • Έλλειμμα κολποκοιλιακού διαφράγματος	• Μέτρια έκπτωση της λειτουργικότητας της αριστερής κοιλίας (ΚΕ 30-45%) • Περιγεννητική μυοκαρδιοπάθεια σε προηγούμενη κύηση χωρίς υπολειμματική δυσλειτουργία της αριστερής κοιλίας • Μηχανικές βαλβίδες • Συστηματική δεξιά κοιλία με καλή ή ήπια επηρεασμένη λειτουργικότητα • Κυκλοφορία Fontan (σε καλή κατάσταση και χωρίς καρδιαγγειακή επιπλοκή) • Μη διορθωμένη κυανωτική συγγενής καρδιοπάθεια • Άλλη σύμπλοκη συγγενής καρδιοπάθεια • Μέτρια στένωση μιτροειδούς βαλβίδας • Σοβαρή ασυμπτωματική στένωση αορτικής βαλβίδας • Μέτρια διάταση της αορτής (40-45mm σε σύνδρομο Marfan ή άλλη κληρονομική πάθηση θωρακικής αορτής, 45-50mm σε δίπτυχη αορτική βαλβίδα, σε σύνδρομο Turner index μέγεθος αορτής 20-25mm/m², <50mm σε τετραλογία Fallot) • Κοιλιακή ταχυκαρδία	• Πνευμονική αρτηριακή υπέρταση • Σοβαρή έκπτωση της λειτουργικότητας της συστηματικής κοιλίας (ΚΕ<30% ή NYHAIII-IV) • Περιγεννητική μυοκαρδιοπάθεια σε προηγούμενη κύηση με υπολειμματική δυσλειτουργία της αριστερής κοιλίας • Σοβαρή στένωση της μιτροειδούς βαλβίδας • Σοβαρή συμπτωματική στένωση της αορτικής βαλβίδας • Συστηματική δεξιά κοιλία με μέτρια ή σοβαρά επηρεασμένη λειτουργικότητα • Σοβαρή διάταση της αορτής (>45mm σε σύνδρομο Marfan ή άλλη κληρονομική πάθηση θωρακικής αορτής, >50mm σε δίπτυχη αορτική βαλβίδα, σε σύνδρομο Turner index μέγεθος αορτής >25mm/m², >50mm σε τετραλογία Fallot) • Σύνδρομο Ehlers-Danlos αγγειακού τύπου • Σοβαρή στένωση ή (επαναστένωση) του ισθμού της αορτής • Κυκλοφορία Fontan με επιπλοκές
Κίνδυνος	Μη αυξημένος κίνδυνος της μητρικής θνητότητας ή καθόλου/ ήπια αυξημένος κίνδυνος νοσηρότητας	Ήπια αυξημένος κίνδυνος της μητρικής θνητότητας ή μέτρια αυξημένος κίνδυνος νοσηρότητας	Μέτρια αυξημένος κίνδυνος της μητρικής θνητότητας ή μέτρια έως σοβαρά αυξημένος κίνδυνος νοσηρότητας	Σημαντικά αυξημένος κίνδυνος της μητρικής θνητότητας ή σοβαρά αυξημένος κίνδυνος νοσηρότητας	Πολύ σημαντικά αυξημένος κίνδυνος της μητρικής θνητότητας ή σοβαρής νοσηρότητας
Ποσοστό καρδιαγγειακών επιπλοκών από τη μητέρα	2.5%-5%	5.7%-10.5%	10%-19%	19%-27%	40%-100%
Συμβουλευτική	Ναι	Ναι	Ναι	Ναι: απαιτείται εξειδικευμένη συμβουλευτική	Ναι: η κύηση αντενδείκνυται, σε περίπτωση κύησης θα πρέπει να συζητηθεί διακοπή της
Φροντίδα κατά την κύηση	Τοπικό νοσοκομείο περιφέρειας	Τοπικό νοσοκομείο περιφέρειας	Νοσοκομείο αναφοράς	Εξειδικευμένο νοσοκομείο για κύηση και καρδιακά νοσήματα	Εξειδικευμένο νοσοκομείο για κύηση και καρδιακά νοσήματα
Ελάχιστος αριθμός επισκέψεων κατά την εγκυμοσύνη	Μία ή δύο	Μία φορά το τρίμηνο	Μία φορά το δίμηνο	Μία φορά το μήνα ή το δίμηνο	Μία φορά το μήνα
Νοσοκομείο για τον τοκετό	Τοπικό νοσοκομείο	Τοπικό νοσοκομείο	Νοσοκομείο αναφοράς	Εξειδικευμένο νοσοκομείο για κύηση και καρδιακά νοσήματα	Εξειδικευμένο νοσοκομείο για κύηση και καρδιακά νοσήματα

ΚΕ: κλάσμα εξώθησης

Contraindication for pregnancy (mWHO 4)

	Marfan[19,175]	Bicuspid aortic valve[176]	Loeys Dietz[182-184]	Turner[178,179]	Vascular Ehlers–Danlos[26]
Location of aneurysm/dissection	Everywhere (sinus of Valsalva)	Ascending aorta	Everywhere	Ascending aorta, arch and descending aorta	Everywhere
Risk of dissection	High: 1–10%	Low: <1%	High:1–10%	High: 1–10%	High: 1–10%
Comorbidity	Dural abnormalities Mitral regurgitation Heart failure Arrhythmias	Aortic stenosis or regurgitation	Dural abnormalities Mitral regurgitation	Low height Infertility Hypertension Diabetes Bicuspid aortic valve Coarctation	Dural abnormalities Uterine rupture
Advise not to become pregnant	Ascending aorta >45 mm (or >40 mm in family history of dissection or sudden death)	Ascending aorta >50 mm	Ascending aorta >45 mm (or >40 mm in family history of dissection or sudden death)	ASI >25 mm/m^2	All patients

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Most common cardiac disease groups during pregnancy

www.escardio.org/guidelines

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Heart Diseases during Pregnancy (I)

- Congenital heart disease:
  - most frequent cause of cardiac complications in industrialised countries (70-80%), rare in developing countries (10-20%).
- Valvular disease:
  - most frequent cause of cardiac complications in developing countries (50-90%), 15% in industrialised countries.
- Cardiomyopathies:
  - rare but severe.
- Coronary heart disease:
  - rare but increasing frequency.

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Heart Diseases during Pregnancy (II)

- Hypertension:
  - frequent (6-8% of pregnancies) but severe complications are rare.
- Arrhythmias:
  - frequently combined with stuctural heart disease.
- Venous thromboembolism:
  - deep vein thrombosis,
  - pulmonary embolism.

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Πίνακας 5: Καρδιαγγειακές επιπλοκές κατά τη διάρκεια της κύησης/λοχείας που απαιτούν νοσηλεία

Αίτιο	Διάγνωση	Θεραπεία	Τοκετός
Σοβαρή υπέρταση- Προεκλαμψία	Βιοχημικός έλεγχος αίματος και ούρων	Ενδοφλέβια θεραπεία με λαβηταλόλη, υδραλαζίνη. Νιτρώδη σε περίπτωση πνευμονικού οιδήματος. Από το στόμα θεραπεία με νιφεδιπίνη, λαβηταλόλη, υδραλαζίνη, μεθυλντόπα. Ενδοφλέβιος θειικό μαγνήσιο για πρόληψη της εκλαμψίας.	Φυσιολογικός τοκετός/ Καισαρική τομή
Εν τω βάθει φλεβοθρόμβωση/πνευμονική εμβολή	d-dimers (υψηλή αρνητική προγνωστική αξία) Ακτινογραφία θώρακος Triplex φλεβών κάτω άκρων Σπινθηρογράφημα αιμάτωσης Αξονική αγγειογραφία πνευμονικών αρτηριών με πρωτόκολλο χαμηλής ακτινοβολίας	Αντιηκτική θεραπεία με ηπαρίνη χαμηλού μοριακού βάρους σε θεραπευτική δόση. Θρομβόλυση (ή θρομβεκτομή)σε αιμοδυναμική αστάθεια	Φυσιολογικός τοκετός/ Καισαρική τομή
Καρδιακή ανεπάρκεια	Ηλεκτροκαρδιογράφημα Υπερηχογράφημα καρδιάς Νατριουρητικά πεπτίδια	Πριν τον τοκετό αγωγή καρδιακής ανεπάρκειας (β-αναστολείς, διουρητικά, υδραλαζίνη) χωρίς τερατογόνα φάρμακα (αναστολείς μετατρεπτικού ενζύμου, ανταγωνιστές υποδοχέων αγγειοτενσίνης ΙΙ, ανταγωνιστές των υποδοχέων των αλατοκορτικοειδών). Μετά τον τοκετό προσθήκη όλων των παραπάνω φαρμάκων. Επεμβατική θεραπεία όπου ενδείκνυται. Σε αιμοδυναμική αστάθεια, υστερικα, ενδοκαρδιτιδα αντλία, μεταμόσχευση καρδιάς.	Καισαρική τομή Σε περιπτώσεις σταθερών ασθενών είναι δυνατός φυσιολογικός τοκετός
Πνευμονική αρτηριακή υπέρταση	Ηλεκτροκαρδιογράφημα Υπερηχογράφημα καρδιάς Νατριουρητικά πεπτίδια	Αγγειοδιασταλτικά της πνευμονικής κυκλοφορίας (αναστολείς της φωσφοδιαστεράσης-5, προστανοειδή). Οι ανταγωνιστές υποδοχέων ενδοθηλίνης αντενδείκνυνται.	Καισαρική τομή
Αρρυθμίες	Ηλεκτροκαρδιογράφημα Καταγραφή Holter ρυθμού	**Υπερκοιλιακή ταχυκαρδία**: Ανάταξη με χειρισμούς ή αδενοσίνη. Ηλεκτρική ανάταξη σε αιμοδυναμική αστάθεια. **Κοιλιακή μαρμαρυγή/πτερυγισμός**: β-αναστολείς ως αρχική επιλογή για έλεγχο συχνότητας. Ηλεκτρική ανάταξη για έλεγχο ρυθμού σε αιμοδυναμική αστάθεια. Αμιωδαρόνη καλύτερα να αποφεύγεται. Αντιηκτική αγωγή. **Κοιλιακή ταχυκαρδία**: Ηλεκτρική ανάταξη ή φαρμακευτική ανάταξη με β-αποκλειστή, σοταλόλη εκτός από τις περιπτώσεις μακρού QT, προκαϊναμίδη. Ηλεκτρική ανάταξη σε αιμοδυναμική αστάθεια. Μακροχρόνια β-αναστολείς. Μπορεί να επιχειρηθεί κατά την εγκυμοσύνη κατάλυση κοιλιακής αρρυθμίας στο ηλεκτροφυσιολογικό εργαστήριο **Βραδυκαρδία:** Σπάνια ανάγκη τοποθέτησης βηματοδότη	Καισαρική τομή /Φυσιολογικός τοκετός
Οξύ στεφανιαίο σύνδρομο	Ηλεκτροκαρδιογράφημα Δείκτες μυοκαρδιακής νέκρωσης Υπερηχογράφημα καρδιάς Επεμβατική στεφανιογραφία	Επέμβαση αγγειοπλαστική σε έμφραγμα με αποφρακτικές βλάβες των στεφανιαίων(συχνός ο διαχωρισμός). Φαρμακευτική θεραπεία με αντιαιμοπεταλιακά, νιτρώδη και β-αναστολείς. Θρομβόλυση μόνο σε περίπτωση αδυναμίας διενέργειας αγγειοπλαστικής	Καισαρική τομή σε περιπτώσεις πολύ σταθερών ασθενών είναι δυνατός φυσιολογικός τοκετός ένα μήνα μετά το επεισόδιο
Οξύ αορτικό σύνδρομο	Μαγνητική τομογραφία Αξονική τομογραφία	Αυστηρός έλεγχος της αρτηριακής πίεσης με λαβηταλόλη ενδοφλεβίως. Σε διαχωρισμό τύπου Α κατά Stanford χειρουργική θεραπεία. Σε διαχωρισμό αορτής τύπου Β κατά Stanfordκατά κύριο λόγο συντηρητική θεραπεία.	Καισαρική τομή
Αγγειακό εγκεφαλικό επεισόδιο	Μαγνητική τομογραφία εγκεφάλου	Θεραπεία ανάλογα με το αίτιο (αιμορραγία, θρόμβωση, εμβολή)	Φυσιολογικός τοκετός/ Καισαρική τομή

Hypertension

- Most common medical problem in pregnancy

- Complicates about 5-10% of pregnancies:
  - 1-5% of pre-existing hypertension
  - 5-6% of gestational hypertension
  - 1-4% of pre-eclampsia

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Classification of hypertension in pregnancy

Category	*Systolic mmHg*		*Diastolic mmHg*
Normal/ acceptable in pregnancy	≤ 140	and	≤ 90
Hypertension			
Mild	140 - 150	or	90 - 109
Severe	**≥ 160**	or	**≥ 110**

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Classification of hypertension in pregnancy

◆ *Pre-existing hypertension*: either preceding pregnancy or developing before 20 weeks' gestation; usually persisting for longer than 42 days postpartum; it may be associated with proteinuria.

◆ *Gestational hypertension*: developing after 20 weeks' gestation and resolving, in most cases, within 42 days postpartum.

◆ *Preeclampsia*—gestational hypertension with significant proteinuria (≥0.3 g/24 h or ≥30 mg/mmol urinary creatinine in a spot random urine sample); occurring more frequently during the first pregnancy, in multiple fetuses, hydatidiform mole, antiphospholipid syndrome, pre-existing hypertension, renal disease, or in diabetes; is associated with placental insufficiency, often resulting in fetal growth restriction; the only solution is delivery.

◆ *Pre-existing hypertension plus superimposed gestational hypertension with proteinuria.*

◆ *Antenatally unclassifiable hypertension*: term used when BP is first recorded after 20 weeks' gestation and hypertension is diagnosed; re-assessment is necessary at or after 42 days postpartum.

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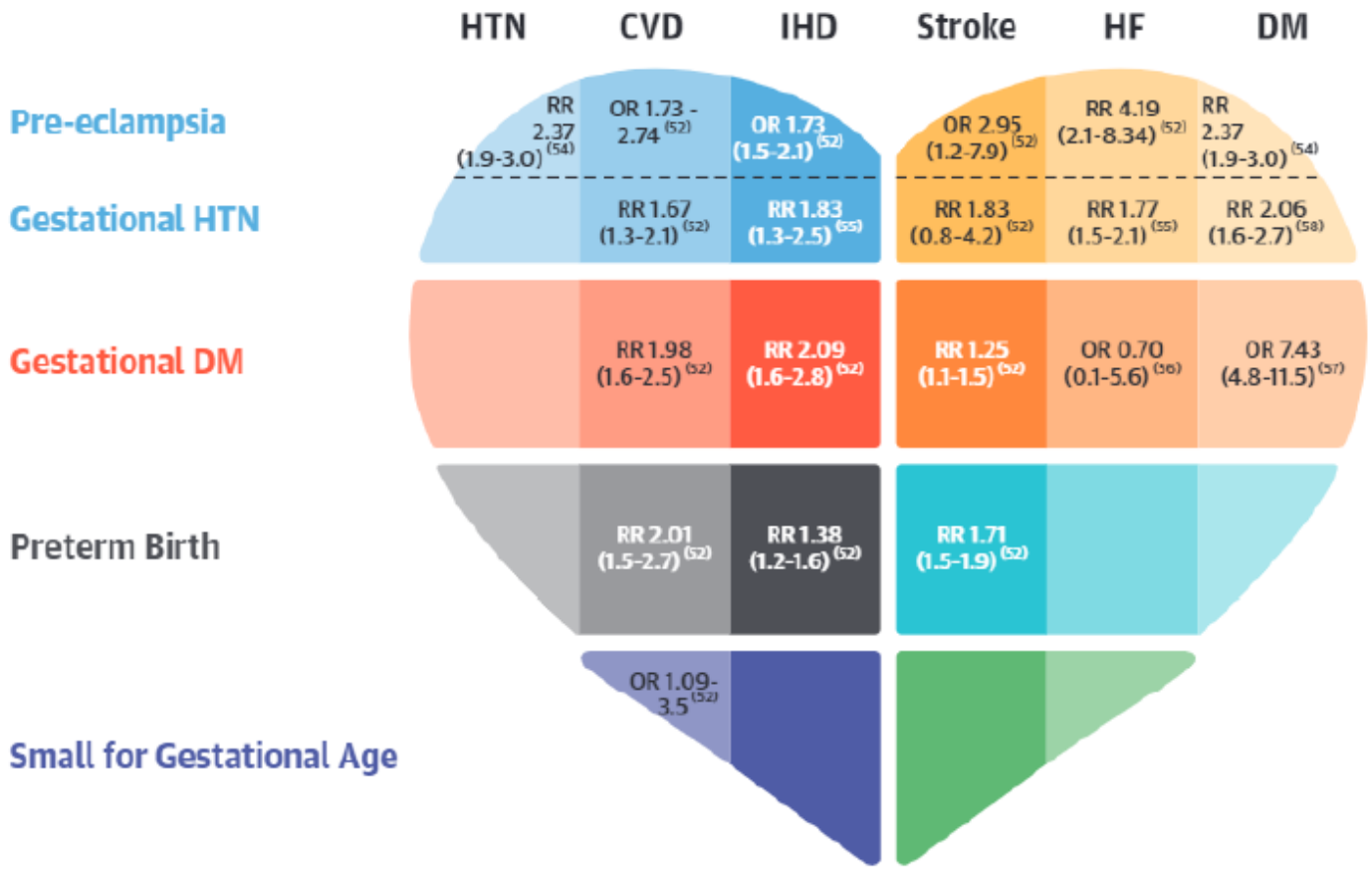
APOs and Future Cardiovascular Risk



Displayed are the pooled risks of future CVD and CVD risk factor development from systematic reviews of APOs including hypertensive disorders of pregnancy (pre-eclampsia and gestational hypertension), gestational DM, preterm birth, and small for gestational age. **Blank spaces** indicate the data have not been synthesized in a published systematic review. **Values in parentheses** are 95% confidence intervals. **Superscript numbers** indicate corresponding reference. APO = adverse pregnancy outcome; CVD = cardiovascular disease composite; DM = diabetes mellitus; HF = heart failure; HTN = hypertension; IHD = ischemic heart disease; OR = odds ratio; RR = relative risk.

Melinda B. Davis et al. *J Am Coll Cardiol* 2021; 77:1763-1777

Pre- excisting Hypertension

- 1-5% of pregnancies
- BP > 140/90 mmHg *predates pregnancy or develops before 20 weeks of gestation*
- In most cases, hypertension *persists more than 42 days post partum,* it may be associated with proteinuria

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Gestational Hypertension

Pregnancy-induced hypertension with or without proteinuria

Hypertension develops ***after 20 weeks´ gestation***,
in most cases, *it resolves within 42 days post partum*

Poor organ perfusion

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Pre-eclampsia

Gestational hypertension associated with *significant proteinuria*

- > 0.3 g/24 h or
- ACR ≥ 30 mg/mmol

Poor organ perfusion

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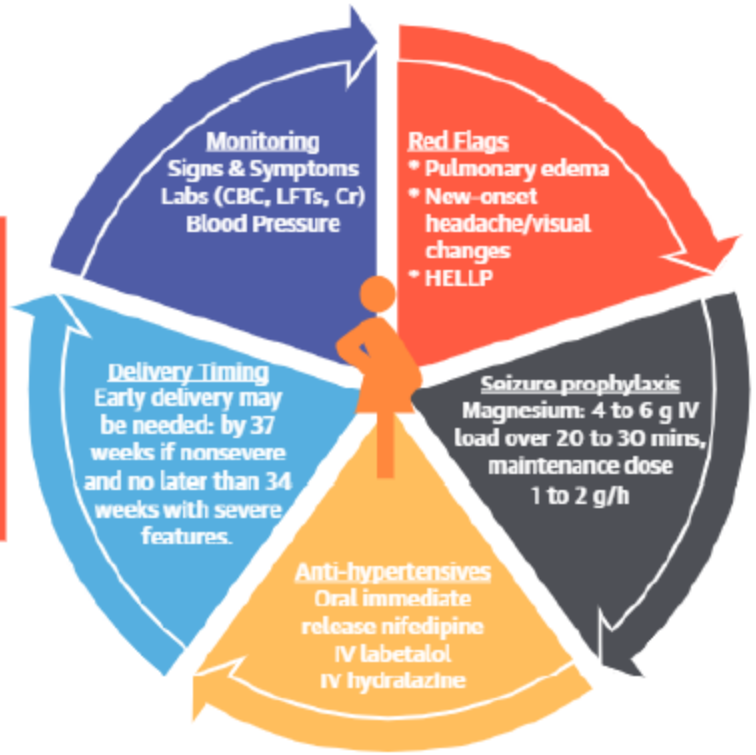
Management of Severe Hypertension/Pre-Eclampsia During Pregnancy and in the Early Postpartum Period

Severe Features of Pre-eclampsia
- BP ≥160 and/or 110 mm Hg
- Thrombocytopenia (<100 x 10^9/L)
- LFTs >2x ULN or Persistent RUQ/epigastric pain
- Renal Insufficiency
- Pulmonary Edema
- New headache
- Visual disturbances



Diagnostic Criteria for HELLP

LDH ≥600 IU/l
AST and ALT >2x ULN
Platelets <100 x 10^9/l

mg Concentration (mg/dl)	Clinical Effect
5-9	Therapeutic range
>9	Loss of reflexes
>12	Respiratory paralysis
>30	Cardiac arrest

Severe hypertension/pre-eclampsia is a medical emergency and requires prompt recognition and treatment. If this occurs during pregnancy, early delivery may be indicated. ALT = alanine aminotransferase; AST = aspartate aminotransferase; BP = blood pressure; CBC = complete blood count; Cr = creatinine; HELLP = hemolysis, elevated liver enzymes, low platelet count; IV = intravenous; LDH = lactate dehydrogenase; LFT = liver function test; RUQ = right upper quadrant; ULN = upper limits of normal.

Melinda B. Davis et al. *J Am Coll Cardiol* 2021; 77:1763-1777

Management of Hypertension in Pregnancy

depends on

- BP levels
- gestational age
- associated maternal and fetal risk factors

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Management of Hypertension in Pregnancy

Dietary and lifestyle interventions

- minimal effect on pregnancy outcome

Regular exercise

- might be continued with caution

Obese women

- are advised to avoid a weight gain of more than 6.8 kg

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Management of Hypertension in Pregnancy

- There is general consensus severe hypertension in pregnancy (≧ 160/110 mmHg) should be treated by antihypertensive drugs
- However, there is no evidence drug treatment of mild-to-moderate hypertension in pregnancy is beneficial (no difference in outcome of preeclampsia, neonatal death, pre-term birth, small-for-gestational-age babies)
- Limitations in study design (small number of participants, no longitudinal outcome)

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Management of Hypertension in Pregnancy

Principles for treatment of mild-to-moderate hypertension in pregnancy

The benefits of antihypertensive therapy for mild-to-moderately elevated BP in pregnancy (≤ 160/110 mmHg), either chronic or pregnancy-induced, have not been demonstrated in clinical trials.

- Less risk of developing severe hypertension
- No difference in outcome of preeclampsia, neonatal death, pre-term birth
- No difference in small-for-gestational-age babies

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Management of Hypertension in Pregnancy

ClinicalTrials.gov

Home > Search Results > Study Record Detail

Chronic Hypertension and Pregnancy (CHAP) Project (CHAP)

Arms and Interventions Go to

Arm	Intervention/treatment
Experimental: Anti-hypertensive therapy to goal <140/90 mmHg Labetalol or Nifedipine ER will be used as first-line to achieve goal; if necessary Nifedipine ER or Labetalol will be second-line antihypertensive. Rarely, other antihypertensive medications may also be used	Drug: Anti-hypertensive therapy 1st line anti-hypertensive (Labetalol or Nifedipine ER) started; escalate to maximum dose and a preferred 2nd line medication if needed (nifedipine ER or Labetalol) Other Names: • Normodyne • Trandate • Procardia XL • Adalat
Active Comparator: No anti-hypertensive unless BP is severe (≥160/105 mmHg Antihypertensive therapy given only if BP becomes severe (defined as BP ≥160/105). The lowest dose of anti-hypertensive needed to keep blood pressure below this threshold will be given (1st-line - Labetalol or Nifedipine ER and 2nd-line - Labetalol or Nifedipine ER). Rarely other medications may be used	Other: No anti-hypertensive therapy (unless BP is severe) Treatment will not be started if blood pressure remains <160/105; for blood pressure ≥160/105, treatment with labetalol or Nifedipine ER will be initiated and maintained at lowest dose needed to keep blood pressure under 160/105.

Management of Hypertension in Pregnancy

ClinicalTrials.gov

Home > Search Results > Study Record Detail

Chronic Hypertension and Pregnancy (CHAP) Project (CHAP)

Principal Findings:

The primary outcome, composite of pre-eclampsia with severe features, medically indicated preterm birth at <35 weeks' gestation, placental abruption, or fetal/neonatal death, occurred in 30.2% of the active treatment group vs. 37.0% of the control group ($p < 0.001$).

Secondary outcomes:

- The safety outcome, small-for-gestational-age birth weight below the 10th percentile for gestational age: 11.2% in the active treatment group vs. 10.4% in the control group ($p = 0.56$)
- Pre-eclampsia with severe features: 23.3% in the active treatment group vs. 29.1% in the control group
- Fatal/neonatal death: 3.5% in the active treatment group vs. 4.3% in the control group

Interpretation:

Among pregnant women with mild chronic hypertension, antihypertensive therapy targeted to a blood pressure <140/90 mm Hg reduced the incidence of adverse pregnancy outcomes compared with usual care. Active treatment improved outcomes without increasing the risk for low birth weight. A large proportion of non-Hispanic blacks were enrolled in this trial.

Management of Hypertension in Pregnancy

Thresholds for drug treatment initiation

BP > 140/90 mmHg in women with

- gestational hypertension (with or without proteinuria) *or*
- pre-existing hypertension and superimposed gestational hypertension *or*
- hypertension with subclinical organ damage or symptoms at any time during pregnancy

BP > 150/95 mmHg

- in all other circumstances

methyldopa, labetalol, calcium antagonists, and beta-blockers

AVOID: *ACE inhibitors, AIIAs, direct renin inhibitors*, diuretics

magnesium sulfate: eclampsia, treatment and prevention of seizures

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Management of Hypertension in Pregnancy

Thresholds for drug treatment initiation

BP > 140/90 mmHg in women with

- in all other circumstances
  methyldopa, labetalol, calcium antagonists, and beta-blockers

AVOID: *ACE inhibitors, AIIAs, direct renin inhibitors*, diuretics

magnesium sulfate: eclampsia, treatment and prevention of seizures

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Management of Hypertension in Pregnancy

Preconception counselling

- Beta-blockers may induce fetal bradycardia, growth retardation and hypoglycemia; less effective than calcium antagonists

- Type and dose of beta-blockers should be carefully selected
  - most favorable data available for labetalol
  - atenolol best avoided

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Management of Hypertension in Pregnancy

Emergency management of hypertension in pregnancy

- **SBP ≥ 170 or DBP ≥ 110 mmHg**

hydralazine, labetalol, methyldopa or nifedipine, nicardipine, sodium nitroprusside (risk of fatal cyanide poisoning with prolonged treatment), nitroglycerin

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Management of Hypertension in Pregnancy

Conclusions

- In *non-severe hypertension*, oral methyldopa, labetalol, calcium antagonists are drugs of choice
- In pre-eclampsia with pulmonary edema, nitroglycerin is the drug of choice, diuretic therapy is inappropriate because plasma volume is reduced
- As *emergency*, intravenous labetalol, oral methyldopa, and oral nifedipine are indicated. *Intravenous hydralazine is no longer the drug of choice* because of an excess of perinatal adverse effects

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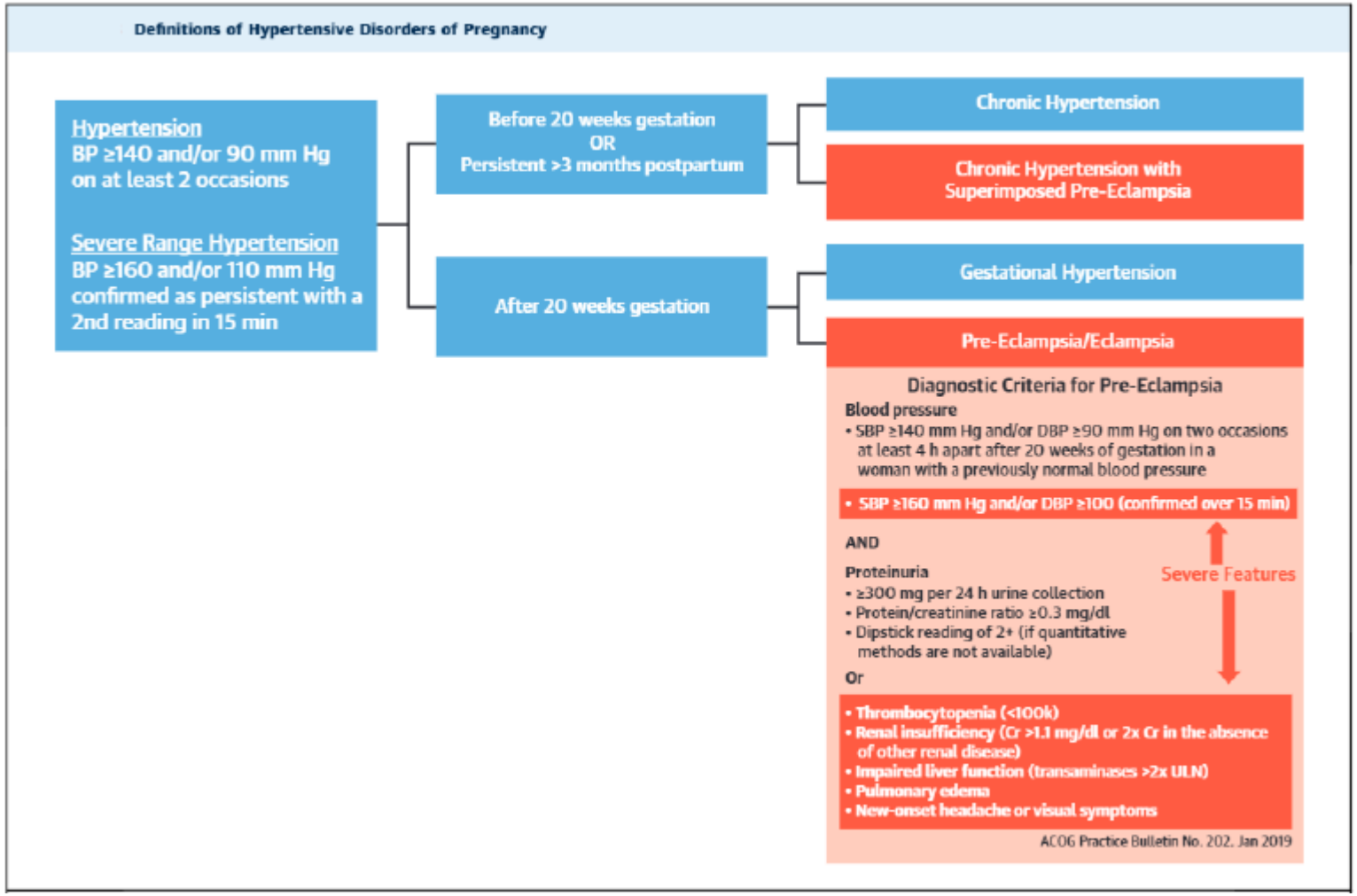

Ki Park et al. *J Am Coll Cardiol* 2021; 77:1799-1812

Preferred Agents for Antihypertensive Treatment in Pregnancy

	Starting Dose	Titration	Maximum Dosage
First line			
Labetalol	100-200 mg by mouth twice daily	Every 2-3 days	2,400 mg/24 h
Nifedipine ER	30-60 mg by mouth every day	Every 7-14 days	120 mg/24 h
Alpha-methyldopa	250 mg by mouth 2 to 3 times daily	Every 2 days	3,000 mg/24 h
Second/third line			
Hydralazine*	10 mg by mouth 4 times daily	Every 2-5 days	300 mg/24 h
Thiazide diuretics	12.5 mg by mouth once a day	Every 7-14 days	50 mg/ 24 h
Clonidine	0.1-0.3 mg by mouth twice a day	Every 7 days	0.6 mg/24 h
	0.1 mg transdermal every day	Every 7-14 days	0.3 mg/24 h
Contraindicated: ACE inhibitor/ARB, renin inhibitors, MRAs			
Intravenous therapies for the urgent treatment of severe hypertension in pregnancy			
Labetalol	10-20 mg intravenously	20-80 mg intravenously every 20-30 min to max 300 mg or 1-2 mg/min intravenous, gtt	
Nifedipine IR	10-20 mg by mouth	Repeat × 1 in 20 min, then 10-20 mg every 2-6 h	
Hydralazine*	5 mg intravenously or intramuscularly	5-10 mg intravenously every 20–40 min or 0.5-10 mg/h intravenous, gtt	

*Do not use in isolation due to potential for reflex tachycardia.

ACE — angiotensin-converting enzyme; ARB — angiotensin receptor blocker, ER — extended release; IR — immediate release; MRA — mineralocorticoid receptor antagonist.

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Antihypertensives and Breast Feeding	
Medication Class	**Preferred Agents**
Calcium-channel blockers	Nifedipine, verapamil, diltiazem
Beta-blockers	Labetalol, metoprolol, and propranolol are preferred
ACE inhibitor	Captopril, enalapril, benazepril, quinapril
Diuretics	Hydrochlorothiazide, spironolactone Safe, can decrease milk production Exception: chlorthalidone due to risk of fetal jaundice, thrombocytopenia, hypoglycemia, and electrolyte abnormalities
Methyldopa	Caution! May exacerbate postpartum depression
ARBs	Insufficient data to recommend their use during breast feeding
Clonidine transdermal patch	Caution! Possible infant/lactation effects

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Anticoagulants for Use in Pregnancy and Lactation

	Advantages	Disadvantages	Special Consideration	Lactation
UFH	UFH does not cross the placenta, has an acute reversal agent (protamine), and is favored for patients with renal failure. UFH is also favored for patients with pulmonary embolism and hemodynamic compromise.	Requires frequent monitoring of PTT to determine therapeutic window.	UFH should be used 36 h before induction or cesarean section because it has a shorter half-life than LMWH. UFH drip should be stopped 4 to 6 h before anticipated delivery and restarted 6 h after delivery if no bleeding complications occur.	UFH is not found in breast milk in any significant amount. There is no contraindication to its use in lactation.
Enoxaparin (LMWH)	Does not cross the placenta, and is convenient for outpatient use. Lower risk of heparin-induced thrombocytopenia, major bleeding, and osteoporosis compared to UFH.	Requires twice daily injections. Higher cost.	Metabolism is primarily by renal excretion, and caution should be used in patients with impaired renal function. As pregnancy progresses there is altered metabolism, and frequent dose adjustments may be required. Follow peak and trough anti-Xa levels meticulously during pregnancy.	Enoxaparin is not found in breast milk in any significant amount; therefore, there is no contraindication to its use in lactation.
Fondaparinux	Fondaparinux is associated with minimal transplacental passage. Recommended by ACOG in the setting of heparin-induced thrombocytopenia or heparin allergy.	Few data on its use in pregnancy are available.		
VKAs	Pregnant women can be switched back to warfarin in the second and third trimesters until delivery.	Crosses the placenta and is a known teratogen. Administration >5 mg/day associated with neurodevelopmental deficits, fetal bleeding, and miscarriage.	Women who are taking VKAs before pregnancy generally need to be switched to LMWH as soon as pregnancy is confirmed, with very few exceptions. An alternative approach is switching to LMWH before conception.	Warfarin is not found in breast milk in any significant amount and can be resumed postpartum.

Direct oral anticoagulants (DOACs) are contraindicated. Rivaroxaban crosses the placental barrier and therefore is contraindicated in pregnancy. Other DOACs have not been evaluated. Pregnant women were excluded from DOAC trials. If a patient has an appropriate indication for anticoagulation, she should be switched to heparin products or warfarin during pregnancy and during lactation.

ACOG — American College of Obstetricians and Gynecologists; LMWH — low-molecular-weight heparin; PTT — partial thromboplastin time; UFH — unfractionated heparin; VKA — vitamin K antagonist.

Nataly Bello et al. *J Am Coll Cardiol* 2021; 77:1813-1822

Table 16 Management of hypertension (1)

Recommendations	Class	Level
Low-dose aspirin (100–150 mg daily) is recommended in women at high or moderate risk of pre-eclampsia from week 12 to weeks 36-37.	I	A
In women with gestational hypertension or pre-existing hypertension superimposed by gestational hypertension, or with hypertension and sub-clinical organ damage or symptoms, initiation of drug treatment is recommended at SBP >140 mmHg or DBP >90 mmHg. In all other cases, initiation of drug treatment is recommended if SBP ≥150 mmHg or DBP ≥95 mmHg.	I	C
SBP ≥170 mmHg or DBP ≥110 mmHg in a pregnant woman is an emergency, and hospitalization is recommended.	I	C
Methyldopa, labetalol, and calcium antagonists are recommended for the treatment of hypertension in pregnancy.	I	B

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Table 16 Management of hypertension (2)

ESC European Society of Cardiology

Recommendations	Class	Level
In women with gestational hypertension or mild pre-eclampsia, delivery is recommended at 37 weeks.	I	B
It is recommended to expedite delivery in pre-eclampsia and with adverse conditions such as visual disturbances or haemostatic disorders.	I	C
In pre-eclampsia associated with pulmonary oedema, nitroglycerin given as an intravenous infusion is recommended.	I	C
In severe hypertension, drug treatment with intravenous labetalol, or oral methyldopa or nifedipine, is recommended.	I	C
Weight gain, limited to <6.8 kg for obese pregnant women, should be considered.	IIa	C
ACE inhibitors, ARBs, or direct renin inhibitors are not recommended.	III	C

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Hypertension

- Heterogeneous entity: pre-existing hypertension, gestational hypertension and pre-eclampsia.
- No benefit of treating mild-to-moderate hypertension (< 170/11 160/110 lg).
- Severe hypertension (≥ 1 160/110 mmHg) is an emergency and hospitalisation is recommended (IC).
- Alpha-methyl-dopa is the drug of choice, followed by labetalol. Calcium-channels blockers are drugs of second choice.
- ACE inhibitors, angiotensin II antagonists and direct renin inhibitors are strictly contraindicated in pregnancy.

www.escardio.org/guidelines

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Antihypertensive medication and pregnancy

Centrally-acting agents			
Preferred	**Methyldopa**	Proven safety and efficacy	Depression, liver problem, limited efficacy in BP control
Alternative	**Clonidine**	As methyldopa	Limited data on fetal safety
Beta-blockers			
Preferred	**Labetalol**	Similar but more effective than methyldopa	Neonatal hypoglycemia with high doses
Contraindicated	**Atenolol**	N/A	IUGR
CCB's			
Preferred	**Nifedipine**	Similar but more effective than methyldopa	Interaction with magnesium
Alternative	**Verapamil**	Similar efficacy as other agents	As nifedipine + bradycardia
Direct vasodilators	**Hydralazine**	Efficacious i.v. (?)	Poor safety profile
	Nitroprussid e	Only for life-threatning severe HBP	Poor safety profile
Diuretics	**Thiazide**	Useful in chronic HBP	Volume contraction, electrolyte disturbances (PE?)

Moser M et al J Hypertension 2012
Podymov T et al, Hypertension 2008

Intravenous drugs for the treatment of hypertensive emergencies

Drug	Onset of action	Duration of action	Dose	Contraindications	Adverse effects
Esmolol	1–2 min	10–30 min	0.5–1 mg/kg i.v. bolus; 50–300 μg/kg/min as continuous i.v. infusion	History of 2nd or 3rd degree AV block (and in the absence of rhythm support), systolic heart failure, asthma, and bradycardia	Bradycardia
Metoprolol	1–2 min	5–8 h	2.5–5 mg i.v. bolus over 2 minutes; may repeat every 5 minutes to a maximum dose of 15 mg	History of 2nd or 3rd degree AV block, systolic heart failure, asthma, and bradycardia	Bradycardia
Labetalol	5–10 min	3–6 h	0.25–0.5 mg/kg i.v. bolus; 2–4 mg/min continuous infusion until goal BP is reached, thereafter 5–20 mg/h	History of 2nd or 3rd degree AV block, systolic heart failure, asthma, and bradycardia	Bronchoconstriction and foetal bradycardia
Fenoldopam	5–15 min	30–60 min	0.1 μg/kg/min i.v. infusion, increase every 15 min until goal BP is reached with 0.05 to 0.1 μg/kg/min increments		
Clevidipine	2–3 min	5–15 min	2 mg/h i.v. infusion, increase every 2 min with 2 mg/h until goal BP		Headache and reflex-tachycardia
Nicardipine	5–15 min	30–40 min	5–15 mg/h as continuous i.v. infusion, starting dose 5 mg/h, increase every 15–30 min with 2.5 mg until goal BP, thereafter decrease to 3 mg/h	Liver failure	Headache and reflex-tachycardia
Nitroglycerine	1–5 min	3–5 min	5–200 μg/min, 5 μg/min increase every 5 min		Headache and reflex tachycardia
Nitroprusside	Immediate	1–2 min	0.3–10 μg/kg/min, increase by 0.5 μg/kg/min every 5 min until goal BP	Liver/kidney failure (relative)	Cyanide intoxication
Enalaprilat	5–15 min	4–6 h	0.625–1.25 mg i.v.	History of angioedema	
Urapidil	3–5 min	4–6 h	12.5–25 mg i.v. bolus, 5–40 mg/h as continuous infusion		
Clonidine	30 min	4–6 h	150–300 μg i.v. bolus in 5–10 min		Sedation and rebound hypertension
Phentolamine	1–2 min	10–30 min	0.5–1 mg/kg i.v. bolus OR 50–300 μg/kg/min as continuous i.v. infusion		Tachyarrhythmias and chest pain

Hypertension in the Post Partum Period

1. continuation of hypertensive disorders in pregnancy
   - pre-existing hypertension (usually persists > 6 weeks postpartum)
   - gestational hypertension including pre-eclampsia (should resolve within 6 to 12 weeks postpartum)
2. *de novo* pre-eclampsia (headaches, epigastric pain, visual changes, seizures)
3. iatrogenic causes
   - drugs: NSAIDs for analgesia, ergot derivatives for postpartum hemorrhage, or ephedrine
   - hypervolemia (e.g., after regional anesthesia)
4. pain (inadequate analgesia)
5. anxiety

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Hypertension in the Post Partum Period

Advise women with hypertension who wish to breastfeed that their treatment can be adapted to accommodate breastfeeding, and that the need to take antihypertensive medication does not prevent them from breastfeeding. [2019]

Explain to women with hypertension who wish to breastfeed that:

- antihypertensive medicines can pass into breast milk
- most antihypertensive medicines taken while breastfeeding only lead to very low levels in breast milk, so the amounts taken in by babies are very small and would be unlikely to have any clinical effect
- most medicines are not tested in pregnant or breastfeeding women, so disclaimers in the manufacturer's information are not because of any specific safety concerns or evidence of harm.

Make decisions on treatment together with the woman, based on her preferences. [2019]

Hypertension in the Post Partum Period

As antihypertensive agents have the potential to transfer into breast milk:

• consider monitoring the blood pressure of babies, especially those born preterm, who have symptoms of low blood pressure for the first few weeks

• when discharged home, advise women to monitor their babies for drowsiness, lethargy, pallor, cold peripheries or poor feeding. [2019]

- Offer **enalapril** to treat hypertension in women during the postnatal period, with appropriate monitoring of maternal renal function and maternal serum potassium. [2019]

Hypertension in the Post Partum Period

For women of black African or Caribbean family origin with hypertension during the postnatal period, consider antihypertensive treatment with:

- **nifedipine**
- **amlodipine** if the woman has previously used this to successfully control her blood pressure. [2019]

Hypertension in the Post Partum Period

For women with hypertension in the postnatal period, if blood pressure is not controlled with a single medicine, consider a combination of **nifedipine** (or amlodipine) and **enalapril**. If this combination is not tolerated or is ineffective, consider either:

- adding atenolol or labetalol to the combination treatment or
- swapping 1 of the medicines already being used for atenolol or labetalol. [2019]

Hypertension in the Post Partum Period

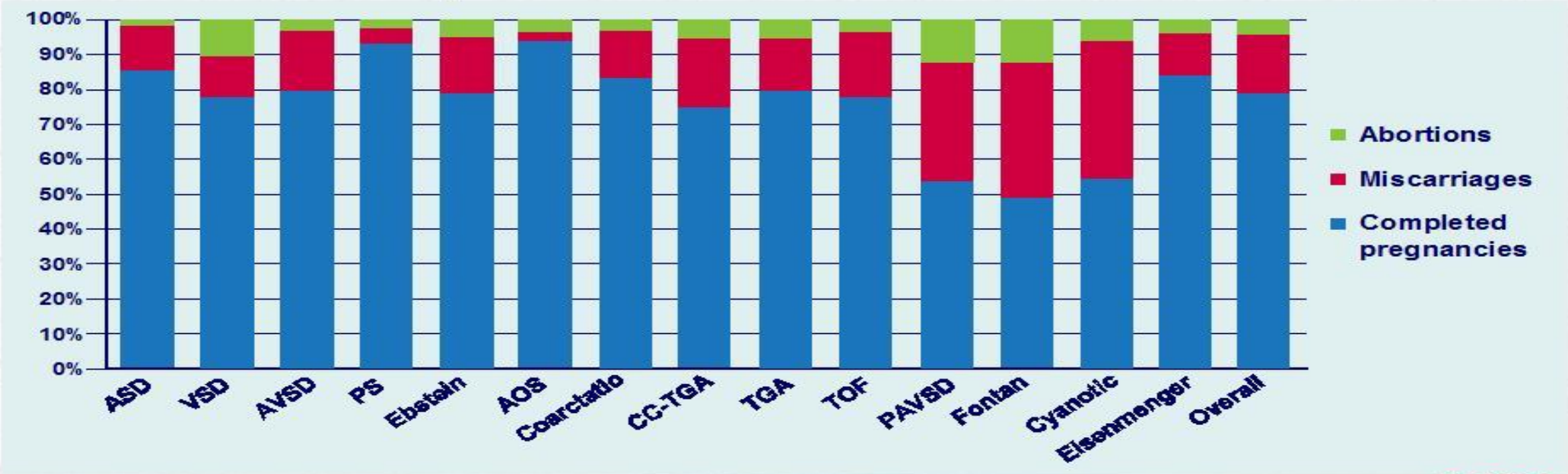
When treating women with antihypertensive medication during the postnatal period, use medicines that are taken once daily when possible. [2019]

Where possible, avoid using diuretics or angiotensin receptor blockers to treat hypertension in women in the postnatal period who are breastfeeding or expressing milk. [2010, amended 2019]

Treat women with hypertension in the postnatal period who are not breastfeeding and who are not planning to breastfeed in line with the NICE guideline on hypertension in adults. [2019]

Congenital Heart Disease

- Risk for fetus depends on the underlying maternal heart disease as well as maternal ventricular and valvular function, functional class, cyanosis, use of anticoagulants.
- Overall fetal mortality 4%.



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Congenital Heart Disease

- Left to right shunts:
  - low to moderate risk.
- Right to left shunts (cyanotic heart disease):
  - moderate risk if previously repaired,
  - high fetal risk if not repaired and O_2 saturation < 85%,
  - major maternal risk (30-50% mortality) if Eisenmenger syndrome contraindication for pregnancy or early termination.
- Obstructions without shunts:
  - high risk if severe left ventricular outflow tract obstruction.

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Low risk patients

- Patients who have undergone previous successful surgical repair for congenital heart disease tolerate pregnancy often well if:
  - no mechanical valve is implanted,
  - the exercise tolerance is good,
  - the ventricular function is normal.

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Pregnancy contraindications in cong. HD

- Women with pulmonary hypertension.
- Women with an oxygen saturation below 85% at rest.
- Patients with transposition of the great arteries and a systemic right ventricle with > moderate impairment of RV function and/or severe TR.
- Fontan patients with depressed ventricular function and/or moderate to severe atrioventricular valvular regurgitation or with cyanosis or with protein losing enteropathy.

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Congenital Heart Diseases (CHD): Essential messages

- Women with CHD may tolerate pregnancy well.
  The risk depends on the underlying specific constellation.
- All patients with CHD should be seen by the end of the first trimester and an individualized follow up plan should be established.
- Vaginal delivery can be planned in most patients.
- Discuss high risk conditions, contraindications and indications for Caesarean delivery on an individual basis.

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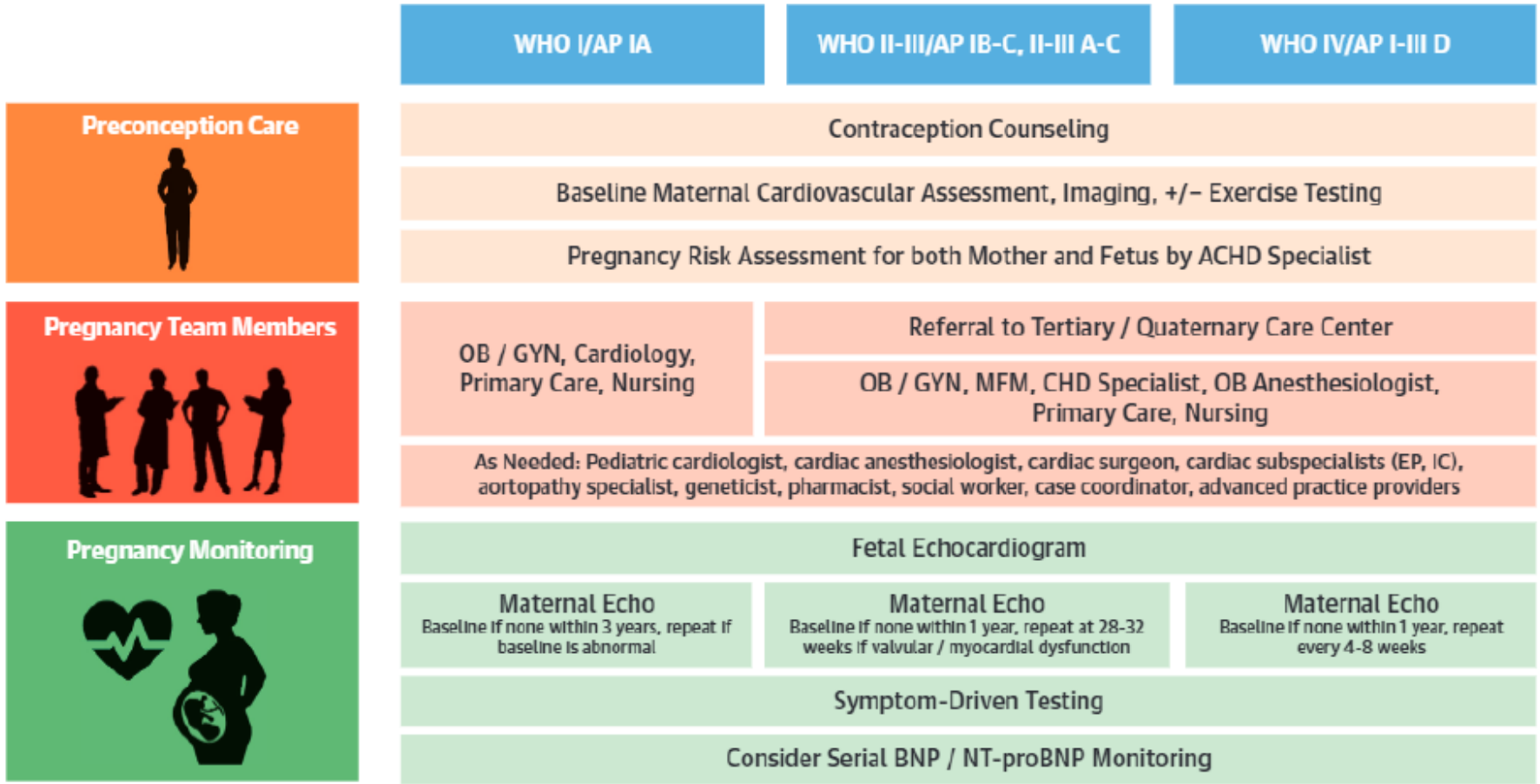
CENTRAL ILLUSTRATION **Multidisciplinary Cardio-Obstetrics Team Management for Women with Congenital Heart Disease**



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

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

Predictors of maternal and neonatal events

Predictors of maternal cardiovascular events	Predictors of neonatal events
Prior cardiac event (heart failure, transient ischaemic attack, stroke, arrhythmia)	NYHA class III/IV or cyanosis during baseline pre-natal visit
NYHA class III/IV	Maternal left heart obstruction
Left heart obstruction (moderate to severe)	Smoking during pregnancy
Reduced systemic ventricular systolic function (ejection fraction <40%)	Low maternal oxygen saturation (<90%)
Reduced subpulmonary ventricular function	Multiple gestations Use of anticoagulants throughout pregnancy
Systemic atrioventricular valve regurgitation (moderate to severe)	Cardiac medication before pregnancy 'At birth' cyanotic heart disease

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Predictors of maternal and neonatal events

Predictors of maternal cardiovascular events	Predictors of neonatal events
Pulmonary atrioventricular valve regurgitation (moderate to severe) Pulmonary arterial hypertension Cardiac medication before pregnancy Cyanosis (O2 <90%) [29,49] Natriuretic peptide levels (NT-proBNP >128 pg/mL at 20 weeks predictive of event later in pregnancy) Smoking history Mechanical valve prosthesis Repaired or unrepaired cyanotic heart disease	Mechanical valve prosthesis Maternal cardiac event during pregnancy Maternal decline in cardiac output during pregnancy Abnormal uteroplacental Doppler flow

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Care during pregnancy

- All women with congenital or other possibly genetic heart disease should be offered foetal echocardiography in weeks 19-22 of pregnancy.
- Echocardiography is recommended in any pregnant patient with known cardiac disease (20 weeks) or with unexplained or new cardiovascular signs or symptoms. CMR when echo does not provides good images.
- A delivery plan should be made between 20-30 weeks of pregnancy detailing induction, management of labour, delivery, and post-partum surveillance.
- When anticoagulation is indicated: Low molecular weight heparin should only be used when weekly monitoring of anti-Xa levels is available.

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Diseases of the Aorta

	Marfan[19,175]	Bicuspid aortic valve[176]	Loeys Dietz[182-184]	Turner[178,179]	Vascular Ehlers–Danlos[26]
Location of aneurysm/dissection	Everywhere (sinus of Valsalva)	Ascending aorta	Everywhere	Ascending aorta, arch and descending aorta	Everywhere
Risk of dissection	High: 1–10%	Low: <1%	High:1–10%	High: 1–10%	High: 1–10%
Comorbidity	Dural abnormalities Mitral regurgitation Heart failure Arrhythmias	Aortic stenosis or regurgitation	Dural abnormalities Mitral regurgitation	Low height Infertility Hypertension Diabetes Bicuspid aortic valve Coarctation	Dural abnormalities Uterine rupture
Advise not to become pregnant	Ascending aorta >45 mm (or >40 mm in family history of dissection or sudden death)	Ascending aorta >50 mm	Ascending aorta >45 mm (or >40 mm in family history of dissection or sudden death)	ASI >25 mm/m^2	All patients

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Aortic diseases - Delivery

Ascending aorta diameter

• < 40 mm	Vaginal delivery is favoured.
• 40-45 mm	Decision on individual basis.
• > 45 mm	Caesarean delivery should be considered.

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Valvular Heart Disease (I)

- Stenotic valve disease:
  - high risk of haemodynamic decompensation if:
    - moderate and severe mitral stenosis consider percutaneous intervention during pregnancy if symptoms persist (IIaC),
    - symptomatic aortic stenosis.
  - intervention is indicated before pregnancy (IC).
- Regurgitant valve disease:
  - good prognosis if preserved left ventricular function,
  - medical therapy is recommended (IC),
  - avoid surgery during pregnancy.

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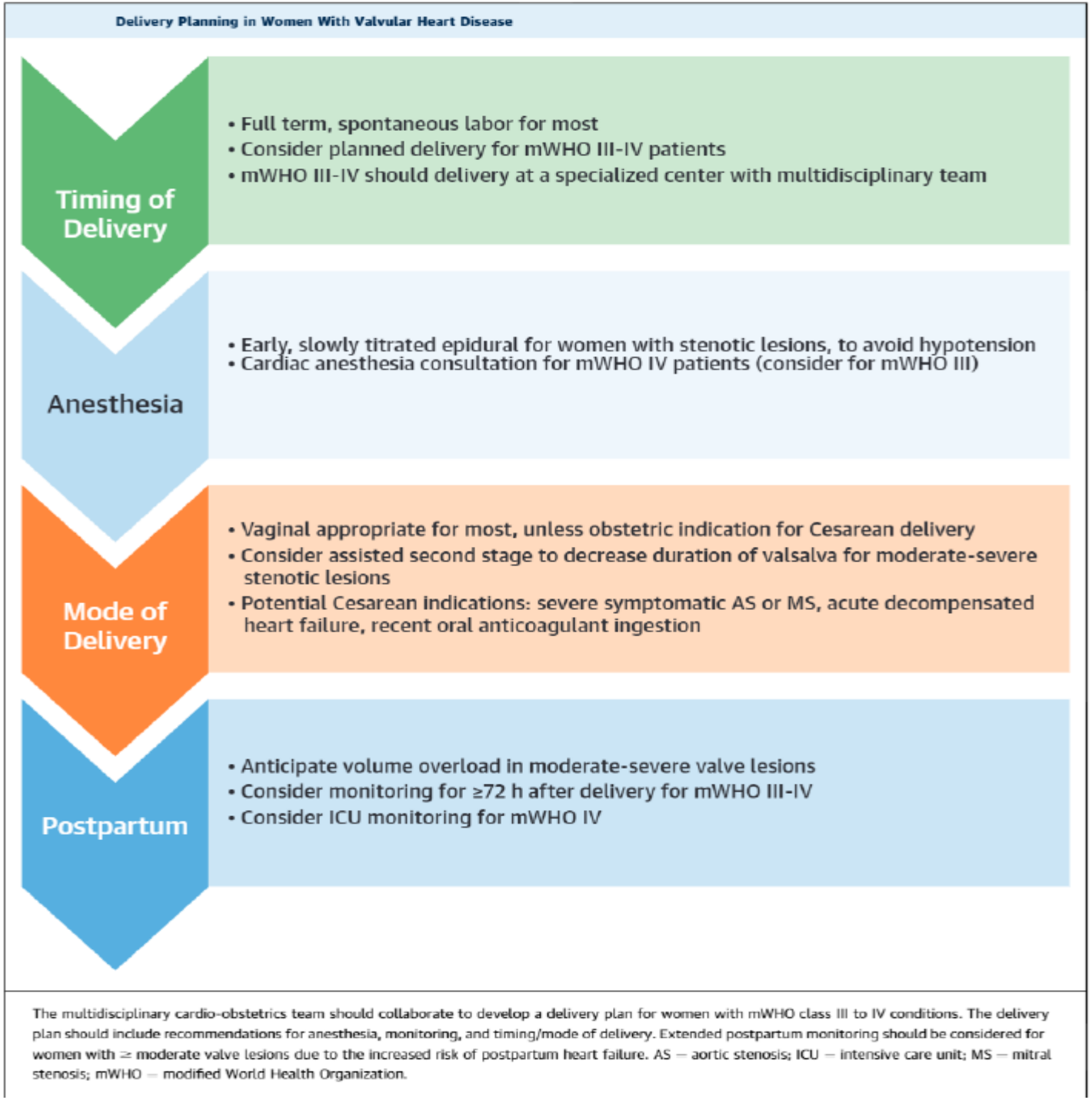


Kathryn J. Lindley et al. *J Am Coll Cardiol* 2021; 77:1778-1798

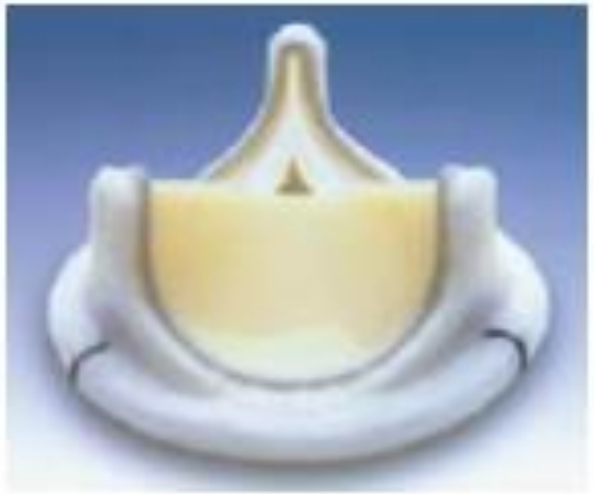
Valvular Heart Disease (II)

Prosthetic valves

- Oral a… with …ts are the sa… t val… re thera… sec… …er (IC).
- Durin… …tinu… be consi… …aily …).
- With … …nts, …-molecular weigh… …nsic… adjustment accor… a le… (IIaC).
- At the… …ld be… …eplaced by do… …C).

Metallic prosthesis

- Longer life
- Need anticoagulation



Bioprosthesis

- No anticoagulation
- Early degeneration
- Risk at reoperation

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Recommendations for the management of valvular heart disease

Mitral stenosis

Recommendations	Class	Level
In patients with symptoms or pulmonary hypertension, restricted activities and ßI-selective blockers are recommended.	I	B
Diuretics are recommended when congestive symptoms persist despite ß-blockers.	I	B
Patients with severe MS should undergo intervention before pregnancy.	I	C
Therapeutic anticoagulation is recommended in the case of atrial fibrillation, left atrial thrombosis, or prior embolism.	I	C
Percutaneous mitral commissurotomy should be considered in pregnant patients with severe symptoms or systolic pulmonary artery pressure > 50 mmHg despite medical therapy.	IIa	C

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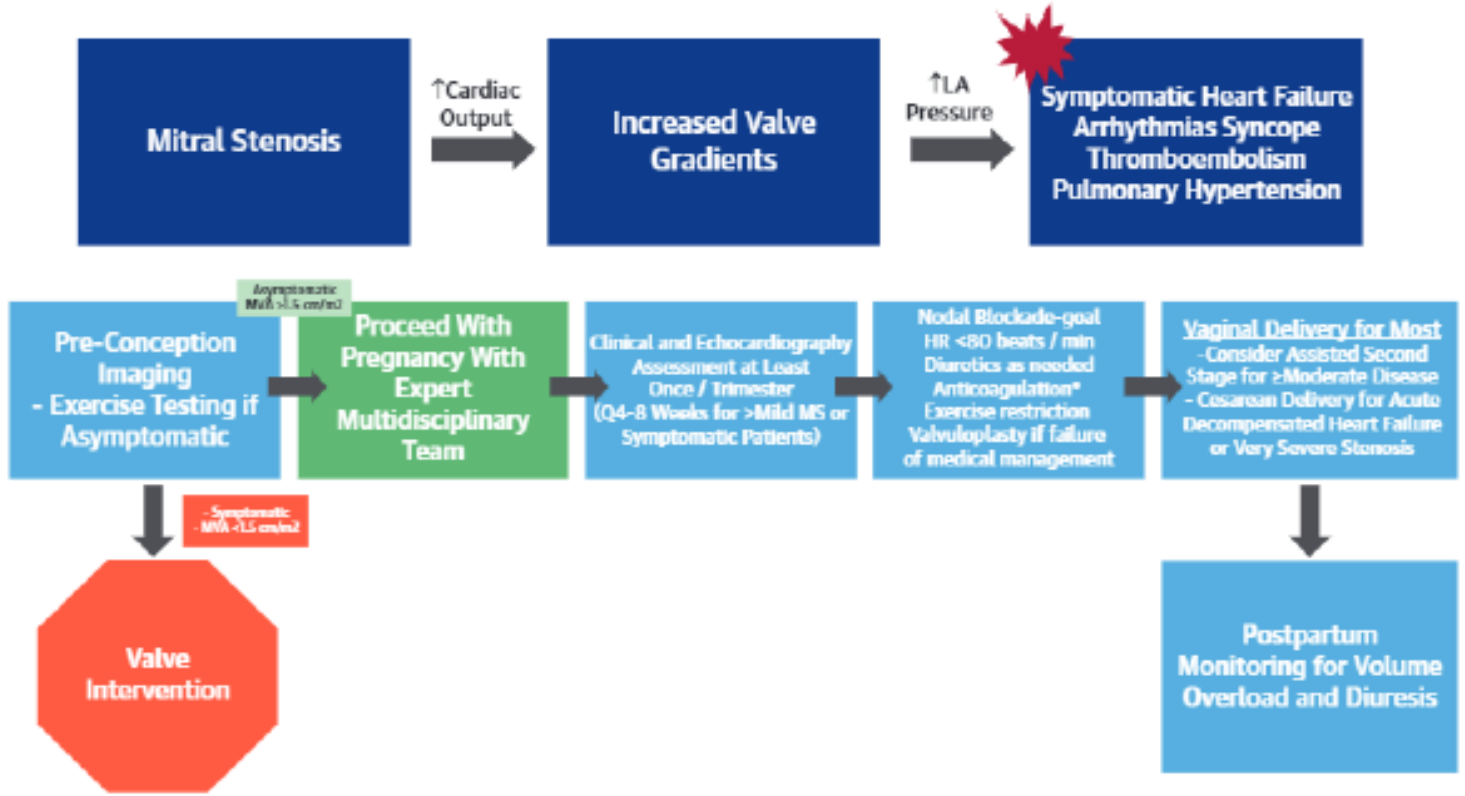
Hemodynamic Changes and Proposed Management Algorithm for Pregnant Women With Mitral Stenosis



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

Kathryn J. Lindley et al. *J Am Coll Cardiol* 2021; 77:1778-1798

Recommendations for the management of valvular heart disease

Aortic stenosis

Recommendations	Class	Level
Patients with severe AS should undergo intervention pre-pregnancy if:		
• the are symptomatic,	I	B
• or LV dysfunction (LVEF < 50%) is present.	I	C
Asymptomatic patients with severe AS should undergo intervention pre-pregnancy when they develop symptoms during exercice testing.	I	C
Asymptomatic patients with severe AS should be considered for intervention pre-pregnancy when a fall in blood pressure below baseline during exercice testing occurs.	IIa	C

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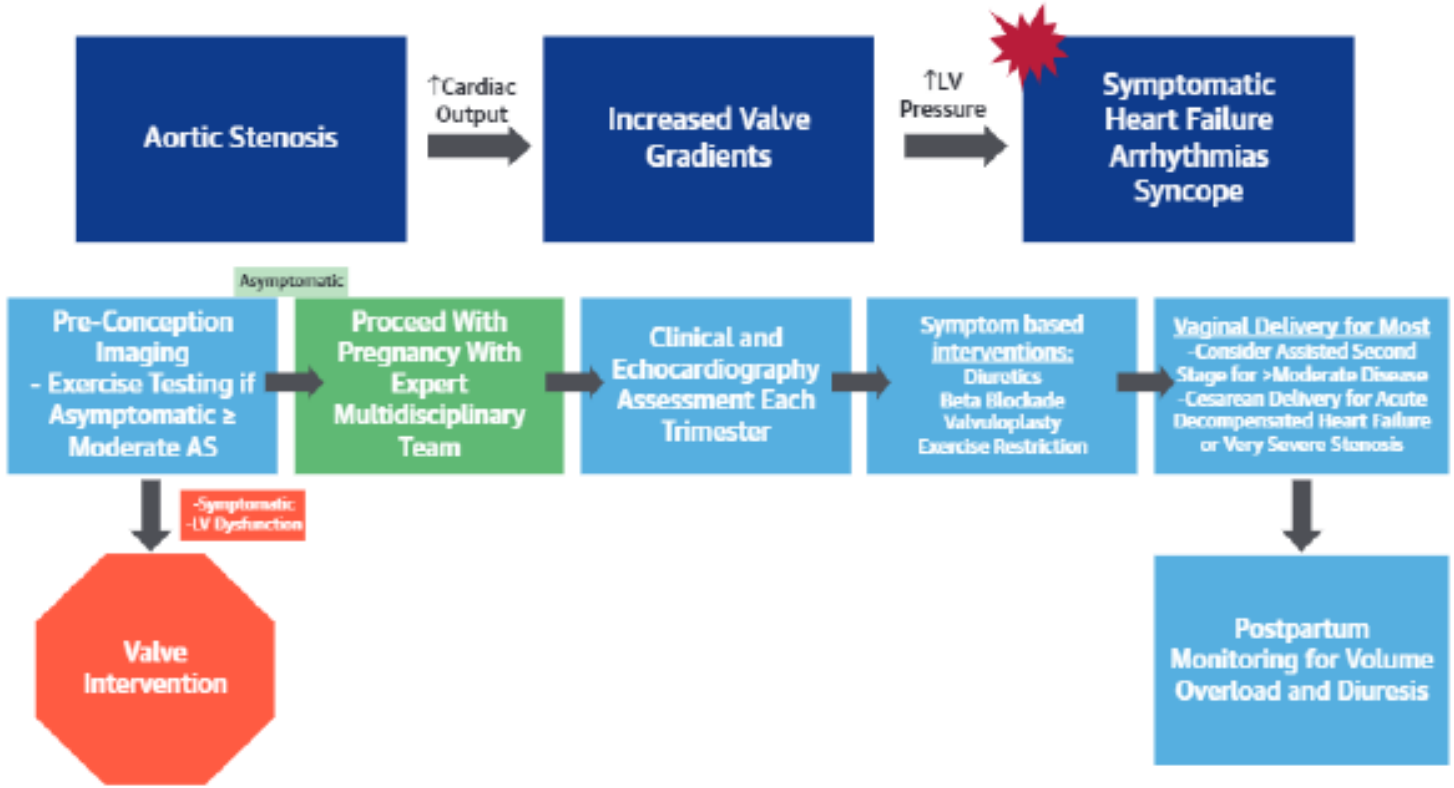
Hemodynamic Changes and Proposed Management Algorithm for Pregnant Women With Aortic Stenosis



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

Kathryn J. Lindley et al. *J Am Coll Cardiol* 2021; 77:1778-1798

Recommendations for the management of valvular heart disease

Regurgitant lesions

Recommendations	Class	Level
Patients with severe aortic or mitral regurgitation and symptoms or impaired ventricular function or ventricular dilatation should be treated surgically pre-pregnancy.	I	C
Medical therapy is recommended in pregnant women with regurgitant lesions when symptoms occur.	I	C

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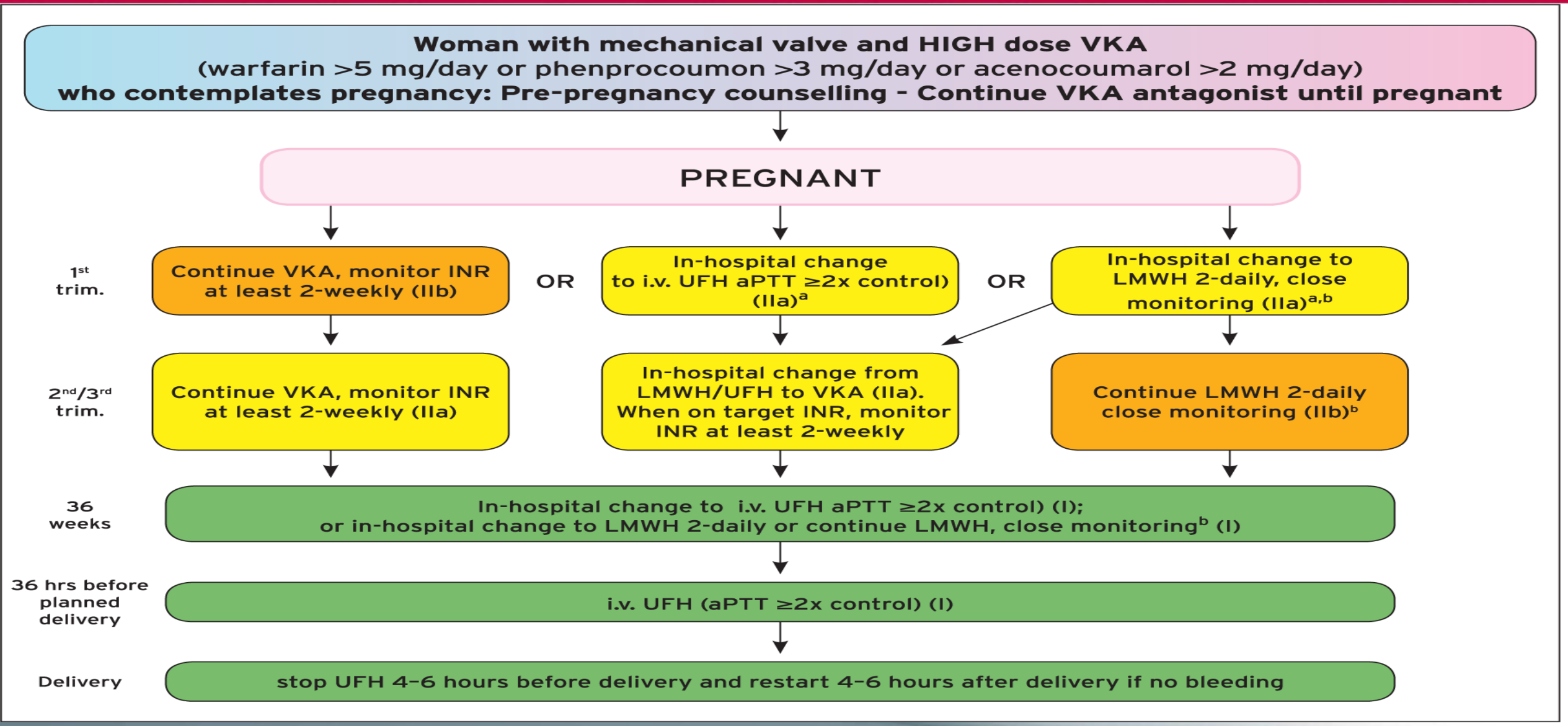
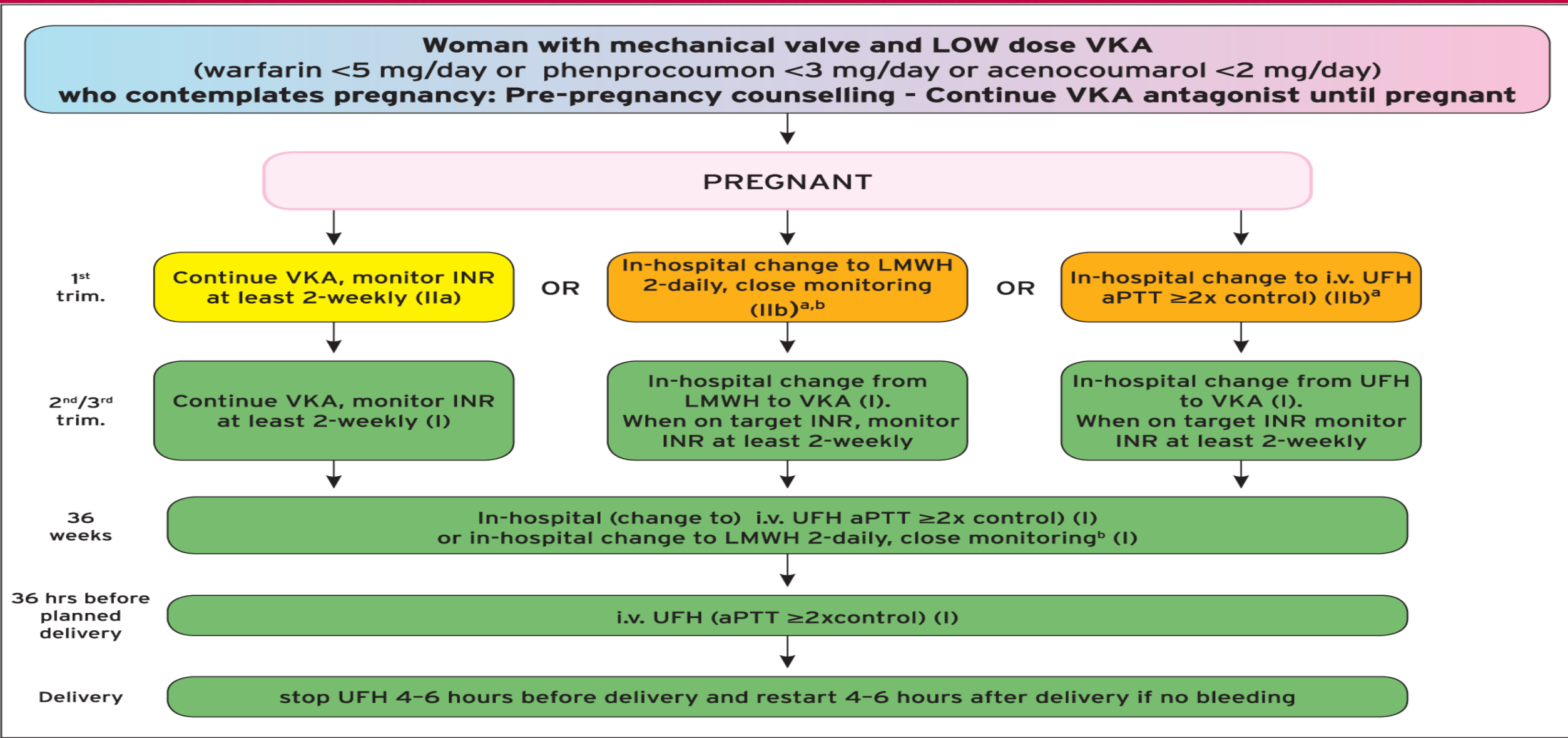
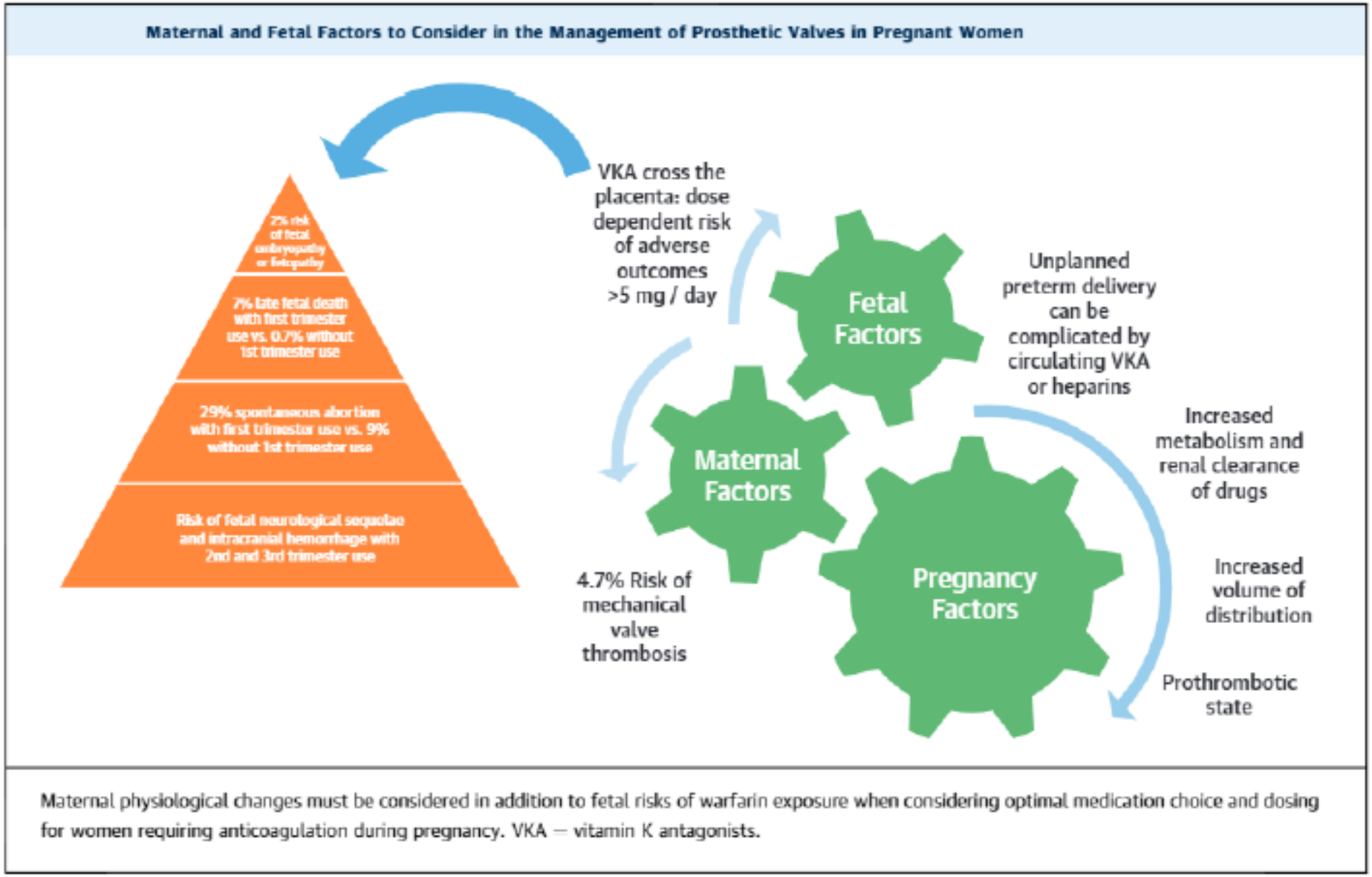
Recommendations for the management of valvular heart disease



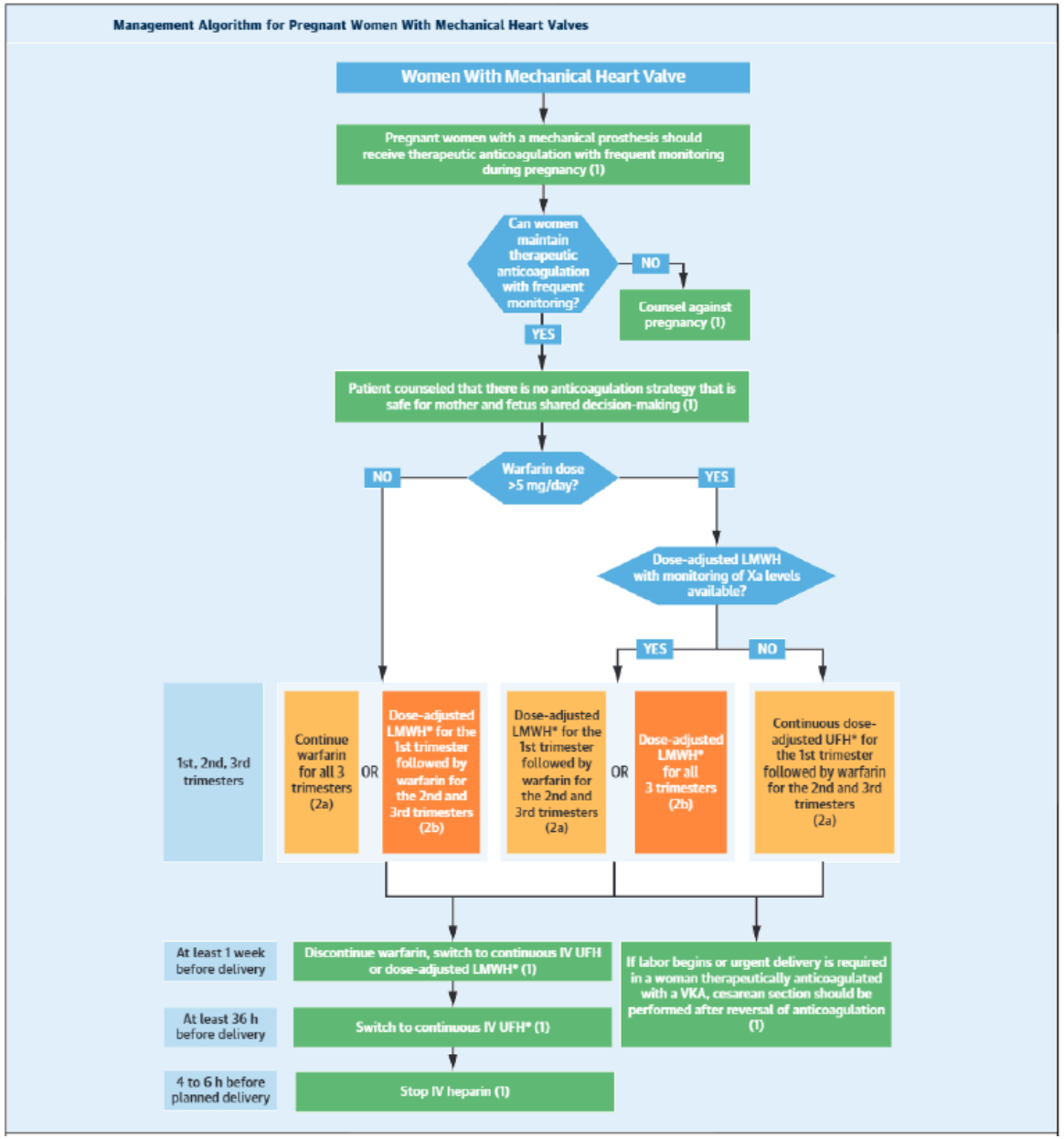
Recommendations for the management of valvular heart disease





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

Kathryn J. Lindley et al. *J Am Coll Cardiol* 2021; 77:1778-1798



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

Kathryn J. Lindley et al. *J Am Coll Cardiol* 2021; 77:1778-1798

Complications of Pregnancy: Infective endocarditis

- The same measures as in non-pregnant patients apply according to recent modifications of guidelines.
- Endocarditis prophylaxis is now only recommended for patients at highest risk to aquire endocarditis and with highest risk procedures.
- Antibiotic prophylaxis is **not** recommended during vaginal or caesarean delivery (IIIC).

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CENTRAL ILLUSTRATION **Management of Complex Acquired and Heritable Cardiovascular Disease in Pregnancy and Considerations for Subspecialty Cardiovascular Care**

	Preconception Assessment	Peripartum Management	Postpartum/Long Term Management
Ischemic Heart Disease	• History of PCI/MI • Evaluate CAD medications • Symptom assessment	• Assessment for possible ACS • Consideration for coronary angiography • Management of antiplatelet therapy	• Contraception • Counseling for consideration of future pregnancies • Long term CVD risk modification
Cardiomyopathy	• History of cardiomyopathy • Evaluate HF medications • Functional class and myocardial reserve	• Acute HF management • Medication adjustment postpartum • Anticoagulation in women with PPCM	
Arrhythmia	• History of implantable device • History of arrhythmia • Assessment of antiarrhythmics, anticoagulation	• Acute management of arrhythmias • Consideration of ablation for acute refractory arrhythmias	
Hypertensive Disorders of Pregnancy	• History of chronic hypertension • Antihypertensive medication adjustment • Prevention of preeclampsia with low dose ASA	• Management of acute and severe hypertension • Medication adjustment postpartum • Postpartum blood pressure monitoring	

Multidisciplinary Expertise: Hypertension, Interventional, Electrophysiology, and Heart Failure

Park, K. et al. J Am Coll Cardiol. 2021;77(14):1799-812.

Cardiovascular subspecialties should be included in the assessment and management of various cardiovascular conditions during pregnancy shown. ACS — acute coronary syndrome; ASA — acetylsalicylic acid or aspirin; CAD — coronary artery disease; CVD — cardiovascular disease; HF — heart failure; MI — myocardial infarction; PCI — percutaneous coronary intervention; PPCM — peripartum cardiomyopathy.

European Heart Journal
doi:10.1093/eurheartj/ehr218

ESC GUIDELINES

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)

Endorsed by the European Society of Gynecology (ESG), the Association for European Paediatric Cardiology (AEPC), and the German Society for Gender Medicine (DGesGM).

Authors/Task Force Members Vera Regitz-Zagrosek (Chairperson) (Germany)*, Carina Blomstrom Lundqvist (Sweden), Claudio Borghi (Italy), Renata Cifkova (Czech Republic), Rafael Ferreira (Portugal), Jean-Michel Foidart† (Belgium), J. Simon R. Gibbs (UK), Christa Gohlke-Baerwolf (Germany), Bulent Gorenek (Turkey), Bernard Iung (France), Mike Kirby (UK), Angela H. E. M. Maas (The Netherlands), Joao Morais (Portugal), Petros Nihoyannopoulos (UK), Petronella G. Pieper (The Netherlands), Patrizia Presbitero (Italy), Jolien W. Roos-Hesselink (The Netherlands), Maria Schaufelberger (Sweden), Ute Seeland (Germany), Lucia Torracca (Italy).

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European Heart Journal
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ESC GUIDELINES

2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy

ESC European Society of Cardiology

The Task Force for the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC).

Endorsed by: the International Society of Gender medicine (IGM), the German Institute of Gender in Medicine (DGesGM), the European Society of Anaesthesiology (ESA), and the European Society of Gynecology (ESG).

Authors/Task Force Members: Vera Regitz-Zagrosek (Chairperson) (Germany), Jolien W. Roos-Hesselink (Co-Chairperson) (The Netherlands), Johann Bauersachs (Germany), Carina Blomström-Lundqvist (Sweden), Renata Cífková (Czech Republic), Michele De Bonis (Italy), Bernard Iung (France), Mark R. Johnson (UK), Ulrich Kintscher (Germany), Peter Kranke (Germany), Irene Marthe Lang (Austria), Joao Morais (Portugal), Petronella G. Pieper (The Netherlands), Patrizia Presbitero (Italy), Susanna Price (UK), Giuseppe M. C. Rosano (UK/Italy), Ute Seeland (Germany), Tommaso Simoncini (Italy), Lorna Swan (UK), Carole A. Warnes (USA).

Why are these guidelines important?

Pregnancy is complicated by maternal disease in 1–4% of cases. CVD are the most common causes of maternal death in Europe. Hypertension affects 5 - 10 % of all pregnant women.

Knowledge of the risks associated with CVDs during pregnancy and their management is of pivotal importance for advising patients before and during pregnancy.

However:

- the number of cases is too small to allow the single physician to rely on her/his own experiences.
- the number of prospective studies is very limited. Most recommendations are class C – expert discussion is needed.

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2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy

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2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy

ESC European Society of Cardiology

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Table 1 Classes of recommendations

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Classes of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended/ is indicated.
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	*Weight of evidence/opinion is in favour of usefulness/efficacy.*	Should be considered.
Class IIb	*Usefulness/efficacy is less well established by evidence/opinion.*	May be considered.
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended.

Table 2 Levels of evidence

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Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

What is new?

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Selected revised recommendations (1)	
Comment/comparison with 2011 version	**2018**
Strengthening mWHO classification of maternal risk.	It is recommended to perform risk assessment in all women with cardiac diseases of childbearing age and before conception, using the mWHO classification of maternal risk (IC).
Upgrade in class of recommendation; patients with severe MS should undergo intervention before pregnancy.	Intervention is recommended before pregnancy in patients with MS and valve area <1.0 cm^2 (IC).
In 2011, OACs were recommended during the second and third trimesters until the 36th week. Now, separate recommendations for women with low and high dose are given for VKA use during the second and third trimesters.	During the second and third trimesters until the 36th week, VKAs are recommended in women needing a low dose (low-dose VKA: warfarin <5 mg/day, phenprocoumon <3 mg/day, or acenocoumarol <2 mg/day) (IC).

What is new?

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Selected revised recommendations (2)	
Comment/comparison with 2011 version	**2018**
Sotalol deleted.	Flecainide or propafenone are recommended for prevention of SVT in patients with WPW syndrome[12] (IC).
Changed in high-risk patients from UFH to LMWH. Dosing based on body weight introduced.	LMWH is the drug of choice for the prevention and treatment of VTE in all pregnant patients (IB). It is recommended that the therapeutic dose of LMWH is based on body weight (IC).
Changes: dose adjustment within 36 h now recommended; added that weekly monitoring is also recommended for UFH.	In pregnant women on LMWH or UFH, it is recommended to perform weekly anti-Xa level monitoring or aPTT monitoring with dose adjustment (within 36 h) (IC).

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What is new?

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Selected revised recommendations (3)	
Comment/comparison with 2011 version	**2018**
Upgrade of recommendation: IIb to IIa.	Catheter ablation with electroanatomical systems should be considered in experienced centres in case of drug-refractory and poorly tolerated SVT (IIaC).
Change from D-dimers to imaging as the first line of investigation, as D-dimers are unreliable in pregnancy.	If compression ultrasound is negative, magnetic resonance venography should be considered to diagnose VTE (IIaC).
FDA categories A–X were used for all drugs in 2011.	FDA categories replaced for new drugs by descriptive risk summary and preclinical safety data (IIIC).

What is new?

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Selected revised recommendations (4)	
Comment/comparison with 2011 version	**2018**
'Pre-pregnancy surgery' is now deleted. Now also information on Turner syndrome with aortic diameter corrected for BSA.	Pregnancy is not recommended in patients with severe dilatation of the aorta (heritable thoracic aortic disease such as Marfan syndrome >45 mm, bicuspid aortic valve >50 mm, >27 mm/m^2 BSA, or Turner syndrome ASI >25 mm/m^2 BSA (IIIC).
Selected new recommendations (1)	
Right heart catheter is recommended to confirm the diagnosis of PAH. This can be performed during pregnancy but with very strict indications[10] (IC).	
Treatment dose LMWH is recommended in pregnant patients with chronic thrombo-embolic pulmonary hypertension (IC).	

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What is new?

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Selected new recommendations (2)
Thrombolytics to manage patients with pulmonary embolism is only recommended in patients with severe hypotension or shock (IC).
In women at high risk for thrombo-embolism, it is recommended to convert LMWH to UFH at least 36 h prior to delivery and stop the UFH infusion 4–6 h prior to anticipated delivery. aPTT should be normal before regional anaesthesia (IC).
In women at low risk for thrombo-embolism on therapeutic LMWH, induction or caesarean section is recommended to be performed 24 h after the last dose of LMWH (IC).
It is recommended to choose the valve prosthesis in women contemplating pregnancy in consultation with a pregnancy heart team (IC).
It is recommended to manage pregnancy in women with mechanical valves in a centre with a pregnancy heart team (IC).

What is new?

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Selected new recommendations (3)
In treatment-naive pregnant PAH patients, initiating treatment should be considered (IIaC).
In patients with (history of) aortic dissection, caesarean delivery should be considered (IIaC).
Beta-blocker therapy throughout pregnancy should be considered in women with Marfan syndrome and other heritable thoracic aortic diseases (IIaC).
Induction of labour should be considered at 40 weeks gestation in all women with cardiac disease (IIaC).
In patients with PPCM, bromocriptine treatment may be considered to stop lactation and enhance recovery (LV function) (IIbB).
Pregnancy is not recommended in patients with vascular Ehlers–Danlos syndrome (IIIC).
Breastfeeding is not recommended in mothers who take antiplatelet agents other than low-dose aspirin (from section 7, see section 12) (IIIC).

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What is new?

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New concepts
Enforcing mWHO classification of maternal risk.
Introduction of the pregnancy heart team.
More attention for assisted reproductive therapy.
Discussion of the use of bromocriptine in PPCM.
Introduction of specific levels of surveillance based on low/medium/high risk for arrhythmia with haemodynamic compromise at delivery.
New information on pharmacokinetics in pregnancy, more detailed information on pharmacodynamics in animal experiments on all drugs (Supplementary data).
Perimortem caesarean section is discussed.
Advice on contraception and the termination of pregnancy in women with cardiac disease is now provided.

Table 4 Predictors of maternal and neonatal events

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Predictors of maternal cardiovascular events	Predictors of neonatal events
Prior cardiac event (heart failure, transient ischaemic attack, stroke, arrhythmia)	NYHA class III/IV or cyanosis during baseline pre-natal visit
NYHA class III/IV	Maternal left heart obstruction
Left heart obstruction (moderate to severe)	Smoking during pregnancy
Reduced systemic ventricular systolic function (ejection fraction <40%)	Low maternal oxygen saturation (<90%)
Reduced subpulmonary ventricular function (TAPSE <16 mm)	Multiple gestations Use of anticoagulants throughout pregnancy
Systemic atrioventricular valve regurgitation (moderate to severe)	Cardiac medication before pregnancy 'At birth' cyanotic heart disease

Table 4 Predictors of maternal and neonatal events

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Predictors of maternal cardiovascular events	Predictors of neonatal events
Pulmonary atrioventricular valve regurgitation (moderate to severe) Pulmonary arterial hypertension Cardiac medication before pregnancy Cyanosis (O2 <90%) [29,49] Natriuretic peptide levels (NT-proBNP >128 pg/mL at 20 weeks predictive of event later in pregnancy) Smoking history Mechanical valve prosthesis Repaired or unrepaired cyanotic heart disease	Mechanical valve prosthesis Maternal cardiac event during pregnancy Maternal decline in cardiac output during pregnancy Abnormal uteroplacental Doppler flow

Table 5 General recommendations (1)

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Recommendations	Class	Level
Pre-pregnancy risk assessment and counselling is indicated in all women with known or suspected congenital or acquired cardiovascular and aortic disease.	I	C
It is recommended to perform risk assessment in all women with cardiac diseases of childbearing age and after conception, using the mWHO classification of maternal risk.	I	C
It is recommended that high-risk patients are treated in specialized centres by a multidisciplinary pregnancy heart team.	I	C
Foetal echocardiography by experienced specialists is recommended when there is an elevated risk of foetal abnormalities.	I	C

Table 5 General recommendations (2)

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Recommendations	Class	Level
Echocardiography is recommended in any pregnant patient with unexplained or new cardiovascular signs or symptoms.	I	C
If cardiac surgery is to be performed after 24 weeks and before 37 weeks of gestation, then corticosteroids are recommended for the mother.	I	C
Vaginal delivery is recommended as the first choice in most patients; for most important exceptions see below.	I	C
Induction of labour should be considered at 40 weeks of gestation in all women with cardiac disease.	IIa	C
Genetic counselling should be considered in women with congenital heart disease or congenital arrhythmia, cardiomyopathies, aortic disease, or genetic malformations associated with CVD.	IIa	C

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Table 5 General recommendations (3)

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Recommendations	Class	Level
MRI (without gadolinium) should be considered if echocardiography is insufficient for a definite diagnosis.	IIa	C
In patients with severe hypertension, vaginal delivery with epidural analgesia and elective instrumental delivery should be considered.	IIa	C
Delivery before necessary surgery should be considered when gestational age is ≥26 weeks.	IIa	C
Caesarean delivery should be considered for obstetrical indications or for patients with dilatation of the ascending aorta >45 mm, severe aortic stenosis, pre-term labour while on oral anticoagulants, Eisenmenger's syndrome, or severe heart failure.	IIa	C

Table 5 General recommendations (4)

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Recommendations	Class	Level
A chest radiograph, with shielding of the foetus, may be considered if other methods are not successful in clarifying the cause of dyspnoea.	IIb	C
Cardiac catheterization may be considered with very strict indications and shielding of the foetus.	IIb	C
CT and electrophysiological studies may be considered in selected patients for vital indications.	IIb	C
Coronary bypass surgery or valvular surgery may be considered during pregnancy when conservative and medical therapy has failed, and in situations that threaten the mother's life or that are not amenable to percutaneous treatment.	IIb	C
Prophylactic antibiotic therapy to prevent endocarditis during delivery is not recommended.	III	C

Table 6 Pregnancy and pulmonary arterial hypertension

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Recommendations	Class	Level
Right heart catheterization is recommended to confirm the diagnosis of PAH (group 1). This can be performed during pregnancy but with very strict indications.	I	C
Treatment dose LMWH is recommended in pregnant patients with chronic thromboembolic pulmonary hypertension.	I	C
If a PAH patient conceives on targeted PH therapies, consideration should be given to withdrawing embryotoxic drugs, taking into account the risks of withdrawal.	IIa	C
In treatment-naive pregnant PAH patients, initiating treatment should be considered.	IIa	C
Pregnancy is not recommended in patients with PAH.	III	B

Table 7 Congenital heart disease

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Recommendations	Class	Level
Patients with a Fontan circulation and saturations <85%, depressed ventricular function, moderate–severe AV regurgitation, refractory arrhythmia, or protein-losing enteropathy should be advised against pregnancy.	IIa	C
Patients with a systemic right ventricle (Mustard/Senning or congenitally corrected TGA), in NYHA class III/IV, systemic ventricular dysfunction (EF <40%), or severe TR should be advised against pregnancy.	IIa	C
Anticoagulation treatment should be considered during pregnancy in Fontan patients.	IIa	C
Symptomatic patients with Ebstein's anomaly with saturations <85% and/or heart failure should be advised against pregnancy.	IIa	C
In patients with a Fontan circulation and saturations <85%, depressed ventricular function, moderate–severe AV regurgitation, refractory arrhythmia, or protein-losing enteropathy, pregnancy is not recommended.	III	C

Table 8 Aortic diseases (1)

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	Marfan	Bicuspid aortic valve	LoeysDietz	Turner	Vascular Ehlers-Danlos
Location of aneurysm/ dissection	Everywhere (sinus of Valsalva)	Ascending aorta	Everywhere	Ascending aorta, arch and descending aorta	Everywhere
Risk of dissection	High: 1–10%	Low: <1%	High:1–10%	High: 1–10%	High: 1–10%
Comorbidity	Dural abnormalities, Mitral regurgitation, Heart failure, Arrhythmias	Aortic stenosis or regurgitation	Dural abnormalities, Mitral regurgitation	Low height, Infertility, Hypertension, Diabetes, Bicuspid aortic valve, Coarctation	Dural abnormalities, Uterine rupture

Table 8 Aortic diseases (2)

	Marfan	Bicuspid aortic valve	LoeysDietz	Turner	Vascular Ehlers-Danlos
Advise not to become pregnant	Ascending aorta >45 mm (or >40 mm in family history of dissection or sudden death)	Ascending aorta >50 mm	Ascending aorta >45 mm (or >40mm in family history of dissection or sudden death)	ASI >25 mm/m^2	All patients

Table 9 Management of aortic disease (1)

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Recommendations	Class	Level
All aortic diseases		
It is recommended that women with aortic disease have counselling about the risk of aortic dissection.	I	C
Imaging of the entire aorta (CT/MRI) is recommended before pregnancy in patients with a genetically proven aortic syndrome or known aortic disease.	I	C
In bicuspid aortic valve patients, imaging of the ascending aorta is recommended before pregnancy.	I	C
When a woman with known aortic dilatation (history of) dissection or genetic predisposition for dissection becomes pregnant, strict blood pressure control is recommended.	I	C

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Table 9 Management of aortic disease (2)

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Recommendations	Class	Level
Repeated echocardiographic imaging every 4–12 weeks (depending on diagnosis and severity of dilatation) is recommended during pregnancy and 6 months post-partum in patients with ascending aorta dilatation.	I	C
For imaging of pregnant women with dilatation of the distal ascending aorta, aortic arch, or descending aorta, MRI (without gadolinium) is recommended.	I	C
It is recommended to deliver all women with aortic dilatation or (history of) aortic dissection in an experienced centre with a pregnancy heart team, where cardiothoracic surgery is available.	I	C
In patients with an ascending aorta <40 mm, vaginal delivery is recommended.	I	C

Table 9 Management of aortic disease (3)

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Recommendations	Class	Level
In patients with an ascending aorta >45 mm, caesarean delivery should be considered.	IIa	C
In patients with (history of) aortic dissection, caesarean delivery should be considered.	IIa	C
Prophylactic surgery should be considered during pregnancy if the aorta diameter is >45 mm and increasing rapidly.	IIa	C
When the foetus is viable, delivery before necessary surgery should be considered.	IIa	C
In patients with an aorta 40–45 mm, vaginal delivery with epidural anaesthesia and an expedited second stage should be considered.	IIa	C

Table 9 Management of aortic disease (4)

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Recommendations	Class	Level
Specific syndromes		
In patients with vascular Ehlers–Danlos syndrome, celiprolol is recommended.	I	C
Beta-blocker therapy throughout pregnancy should be considered in women with Marfan syndrome and other heritable thoracic aortic diseases.	IIa	C
Pregnancy is not recommended in patients with severe dilatation of the aorta (heritable thoracic aortic disease such as Marfan syndrome >45 mm, bicuspid aortic valve >50 mm or >27 mm/m^2 BSA, or Turner syndrome ASI >25 mm/m^2 BSA).	III	C
Pregnancy is not recommended in patients with vascular Ehlers–Danlos syndrome.	III	C

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Figure 2 Flowchart on anticoagulation in mechanical valves and high-dose VKA

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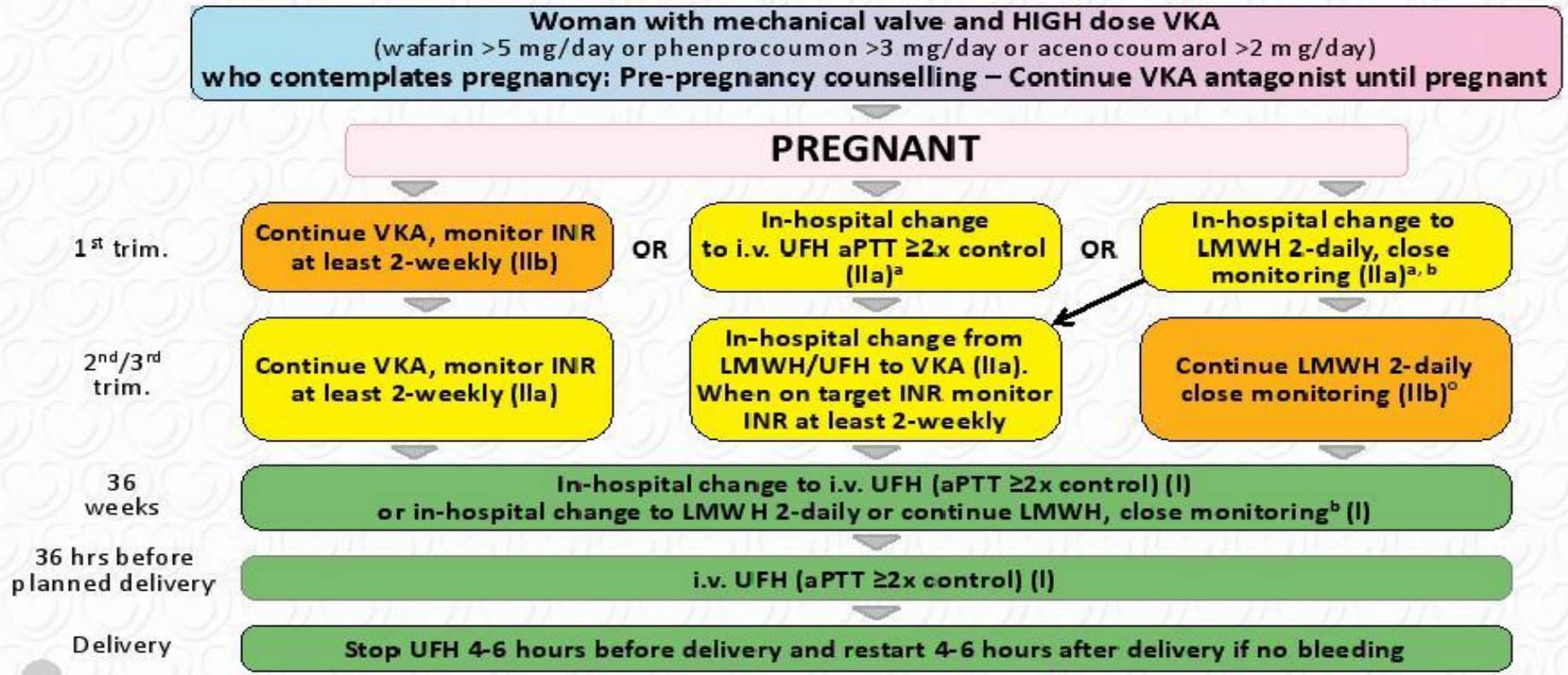

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Figure 3 Flowchart on anticoagulation in mechanical valves and low-dose VKA

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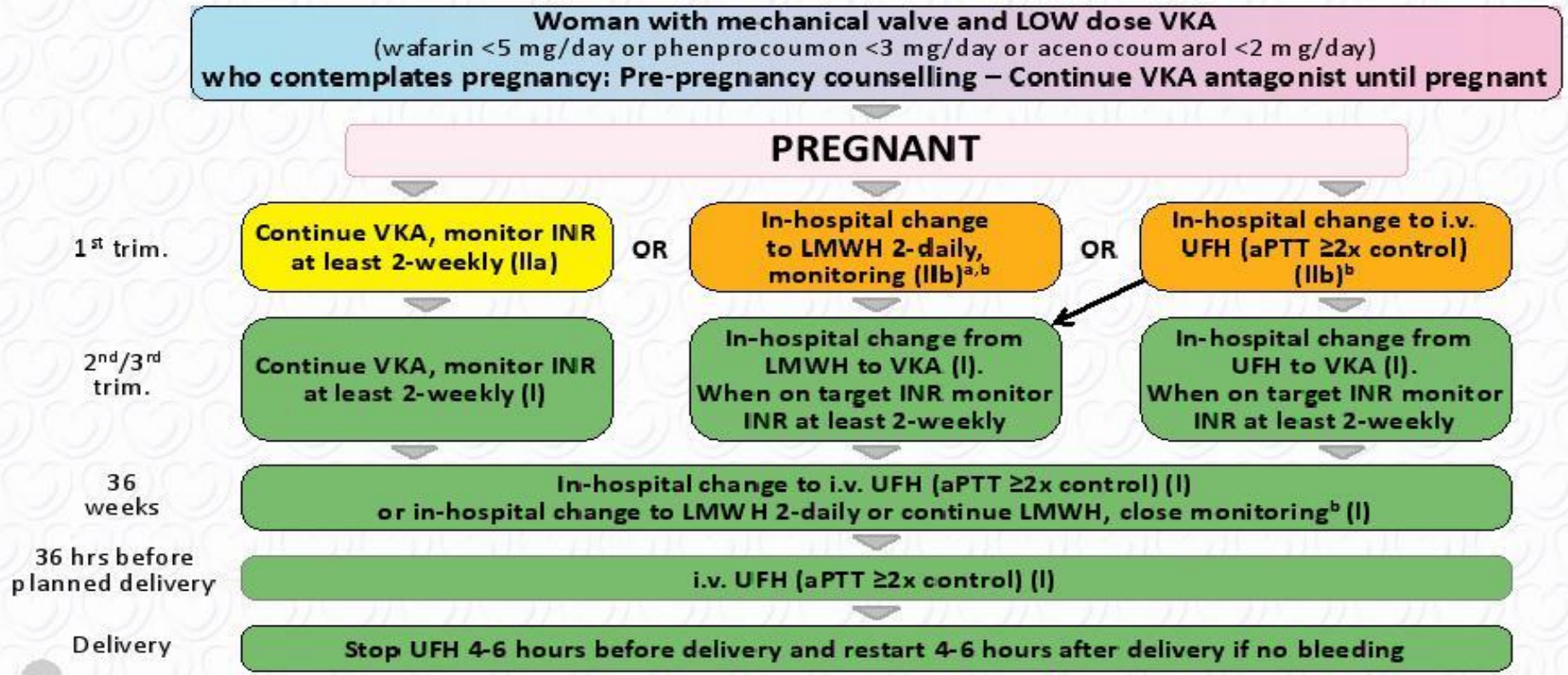

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Figure 4 Flowchart on anticoagulation in mechanical valves and target international normalized ratio for mechanical prostheses

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Prosthesis Thrombogenicity	Risk factors [a]	
	None	≥1
Low [b]	2.5	3.0
Medium [c]	3.0	3.5
High [d]	3.5	4.0

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Table 10 Management of native valvular heart disease (1)

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Recommendations	Class	Level
Pre-pregnancy evaluation, including echocardiography, and counselling is recommended for any woman with known or suspected valvular disease.	I	C
Mitral stenosis		
In patients with symptoms or pulmonary hypertension, restricted activities and beta-1-selective blockers are recommended.	I	B
Diuretics are recommended when congestive symptoms persist despite beta-blockers.	I	B
Intervention is recommended before pregnancy in patients with MS and valve area <1.0 cm^2.	I	C
Therapeutic anticoagulation using heparins or VKA is recommended in case of atrial fibrillation, left atrial thrombosis, or prior embolism.	I	C

Table 10 Management of native valvular heart disease (2)

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Recommendations	Class	Level
Intervention should be considered before pregnancy in patients with MS and valve area <1.5 cm^2.	IIa	C
Percutaneous mitral commissurotomy should be considered in pregnant patients with severe symptoms or systolic pulmonaryartery pressure >50 mmHg despite medical therapy.	IIa	C
Aortic stenosis		
Intervention is recommended before pregnancy in patients with severe aortic stenosis if:		
• they are symptomatic	I	B
• OR LV dysfunction (LVEF <50%) is present	I	C
• OR when they develop symptoms during exercise testing	I	C

Table 10 Management of native valvular heart disease (3)

ESC European Society of Cardiology

Recommendations	Class	Level
Intervention should be considered before pregnancy in asymptomatic patients with severe AS when a fall in blood pressure below baseline during exercise testing occurs.	IIa	C
Balloon aortic valvuloplasty should be considered during pregnancy in patients with severe aortic stenosis and severe symptoms.	IIa	C
Chronic regurgitant lesions		
Surgical treatment is recommended before pregnancy in patients with severe aortic or mitral regurgitation with symptoms of impaired ventricular function or ventricular dilatation.	I	C
Medical therapy is recommended in pregnant women with regurgitant lesions when symptoms occur.	I	C

Table 11 Management of prosthetic heart valves (1)

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Recommendations	Class	Level
It is recommended that the valve prosthesis for a woman contemplating pregnancy is chosen in consultation with a pregnancy heart team.	I	C
It is recommended to manage pregnancy in women with mechanical valves in a centre with a pregnancy heart team.	I	C
If delivery starts while on a VKA or in less than 2 weeks after discontinuation of a VKA, caesarean section is recommended.	I	C
It is recommended to discontinue VKAs and start adjusted-dose intravenous UFH (aPTT ≥2x control) or adjusted-dose LMWH[c] at the 36th week of gestation.	I	C
In pregnant women on LMWH or UFH, it is recommended to perform weekly anti-Xa level monitoring or aPTT monitoring with dose adjustment (within 36 h).	I	C

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Table 11 Management of prosthetic heart valves (2)

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Recommendations	Class	Level
In pregnant women on a VKA, it is recommended to perform INR monitoring weekly or every 2 weeks.	I	C
In pregnant women with LMWH, it is recommended to target anti-Xa levels 4–6 h post-dose at 0.8–1.2 U/l (aortic valve prosthesis) or 1.0–1.2 IU/mL (mitral and right-sided valve prostheses).	I	C
It is recommended to replace LMWH with intravenous UFH (aPTT ≥2x control) at least 36 h before planned delivery. UFH should be continued until 4–6 h before planned delivery and restarted 4–6 h after delivery if there are no bleeding complications.	I	C
It is recommended to anticipate the timing of delivery to ensure safe and effective peripartum anticoagulation.	I	C
Immediate echocardiography is recommended in women with mechanical valves presenting with dyspnoea and/or an embolic event.	I	C

Table 11 Management of prosthetic heart valves (3)

ESC European Society of Cardiology

Recommendations	Class	Level
It is recommended to implement changes in the anticoagulation regimen during pregnancy in hospital.	I	C
During the second and third trimesters until the 36th week, VKAs are recommended in women needing a low dose.[d]	I	C
A bioprosthesis should be considered in young women contemplating pregnancy.	IIa	C
During the second and third trimesters until the 36th week, VKAs should be considered in women needing a high dose.[e]	IIa	C
Continuation of VKAs should be considered during the first trimester if the warfarin dose required for therapeutic anticoagulation is <5 mg/day (or phenprocoumon <3 mg/day or acenocoumarol <2 mg/day) after patient information and consent.	IIa	C

Table 11 Management of prosthetic heart valves (4)

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Recommendations	Class	Level
Discontinuation of VKAs between weeks 6 and 12, and replacement with adjusted-dose intravenous UFH (aPTT ≥2x control) or adjusted-dose LMWH[c] twice daily (see separate recommendations), should be considered in patients with a warfarin dose >5 mg/day (or phenprocoumon >3 mg/day or acenocoumarol >2 mg/day).	IIa	C
During the second and third trimesters, LMWH[c] with anti-Xa level monitoring and dose adjustment (see separate recommendations) may be considered in women who need a high dose of VKA[e] after patient information and consent.	IIb	C
In pregnant women with LMWH, in addition to monitoring peak anti-Xa levels, monitoring pre-dose levels targeted at ≥0.6 IU/mL may be considered.	IIb	C
LMWH is not recommended when weekly anti-Xa level monitoring and dose-adjustment is not available.	III	C

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Coronary Artery Disease

- Acute coronary syndromes:
  - complicate 3-6/100,000 pregnancies,
  - may be due to atherosclerosis but also thrombosis on normal arteries or coronary dissection,
  - should be managed invasively with angiography and percutaneous coronary intervention if indicated, except if non-ST elevation ECG and no risk factors.
- Stable coronary artery disease:
  - pregnancy may be considered in women with known CAD, if there is no residual ischaemia and EF > 40%.

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Coronary Artery Disease

- ACS in pregnancy is rare, complicates 3-6 of 100,000 deliveries.
- ECG and Troponin T levels should be obtained in all women with chest pai (I).
- Spontaneous dissection of coronary arteries is more frequent in pregnant than in non pregnant women.
- Coronary angioplasty is the preferred reperfusion strategy for STEMI (I).
- Pregnancy may be considered in women with known CAD, if there is no residual ischemia and EF > 40%.

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Coronary Artery Disease

Although MI/ACS in pregnancy is relatively uncommon (~ 5 /100 000), CAD accounts for > 20% of all maternal cardiac deaths.

The majority of CAD in pregnancy has non-atherosclerotic mechanisms, i.e. pregnancy-related spontaneous coronary artery dissection (43%), angiographically normal coronary arteries (18%) and coronary thrombosis (17%).

Recommendations	Class	Level
ECG and measurement of troponin levels are recommended when a pregnant woman has chest pain.	I	C
Primary PCI is recommended as the preferred reperfusion therapy for STEMI during pregnancy.	I	C
An invasive management strategy should be considered for NSTE-ACS with risk criteria.	IIa	C
Conservative management should be considered for stable NSTEMI/NSTE-ACS with low risk criteria.	IIa	C
Follow-up should be considered over at least the next 3 months.	IIa	C
Breastfeeding is not recommended in mothers who take anti-platelet agents other than low-dose aspirin due to a lack of data.	III	C

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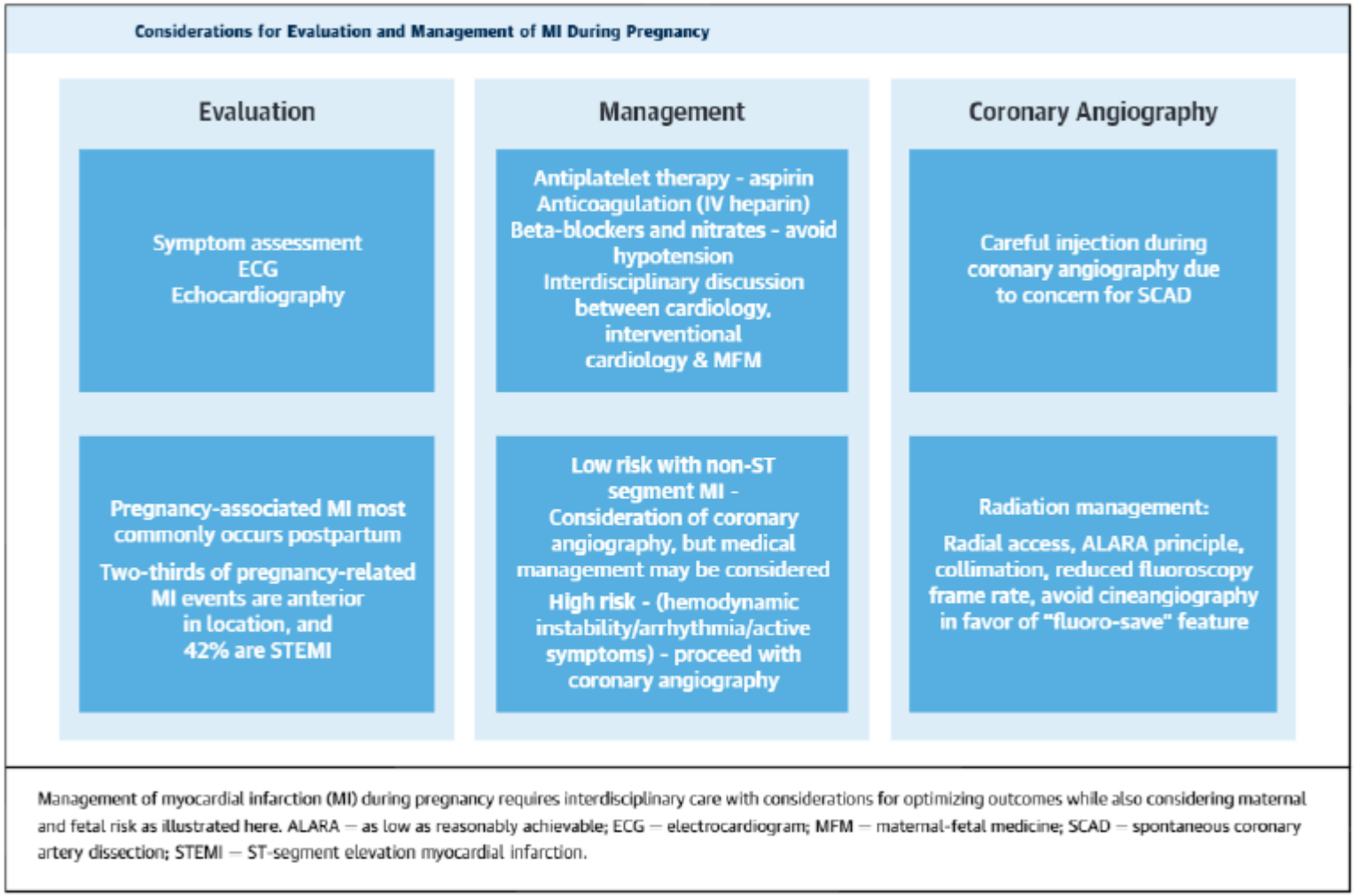

Management of myocardial infarction (MI) during pregnancy requires interdisciplinary care with considerations for optimizing outcomes while also considering maternal and fetal risk as illustrated here. ALARA = as low as reasonably achievable; ECG = electrocardiogram; MFM = maternal-fetal medicine; SCAD = spontaneous coronary artery dissection; STEMI = ST-segment elevation myocardial infarction.

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Ischemic Heart Disease Medications During Pregnancy and Lactation

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

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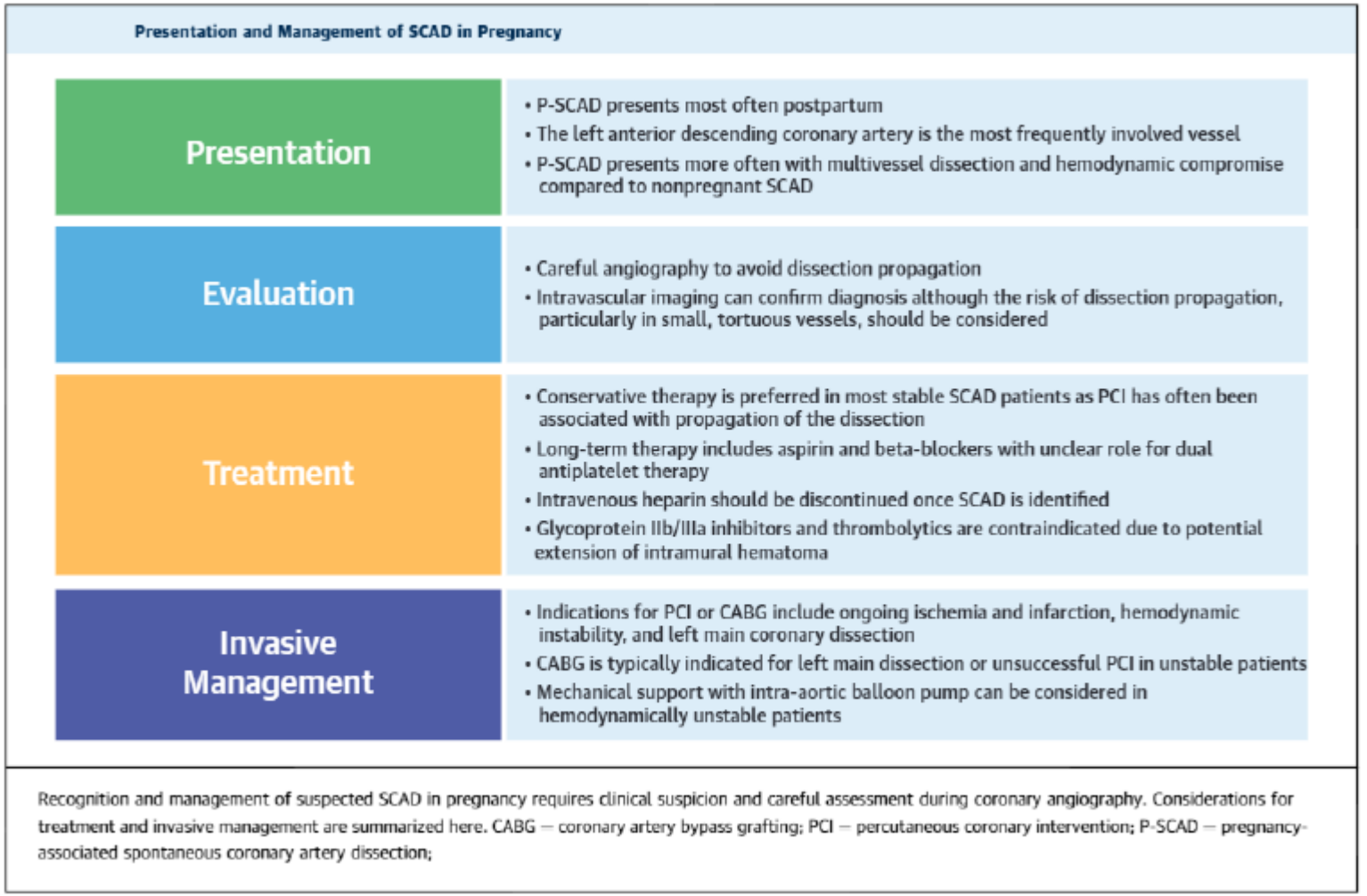

Recognition and management of suspected SCAD in pregnancy requires clinical suspicion and careful assessment during coronary angiography. Considerations for treatment and invasive management are summarized here. CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention; P-SCAD = pregnancy-associated spontaneous coronary artery dissection;

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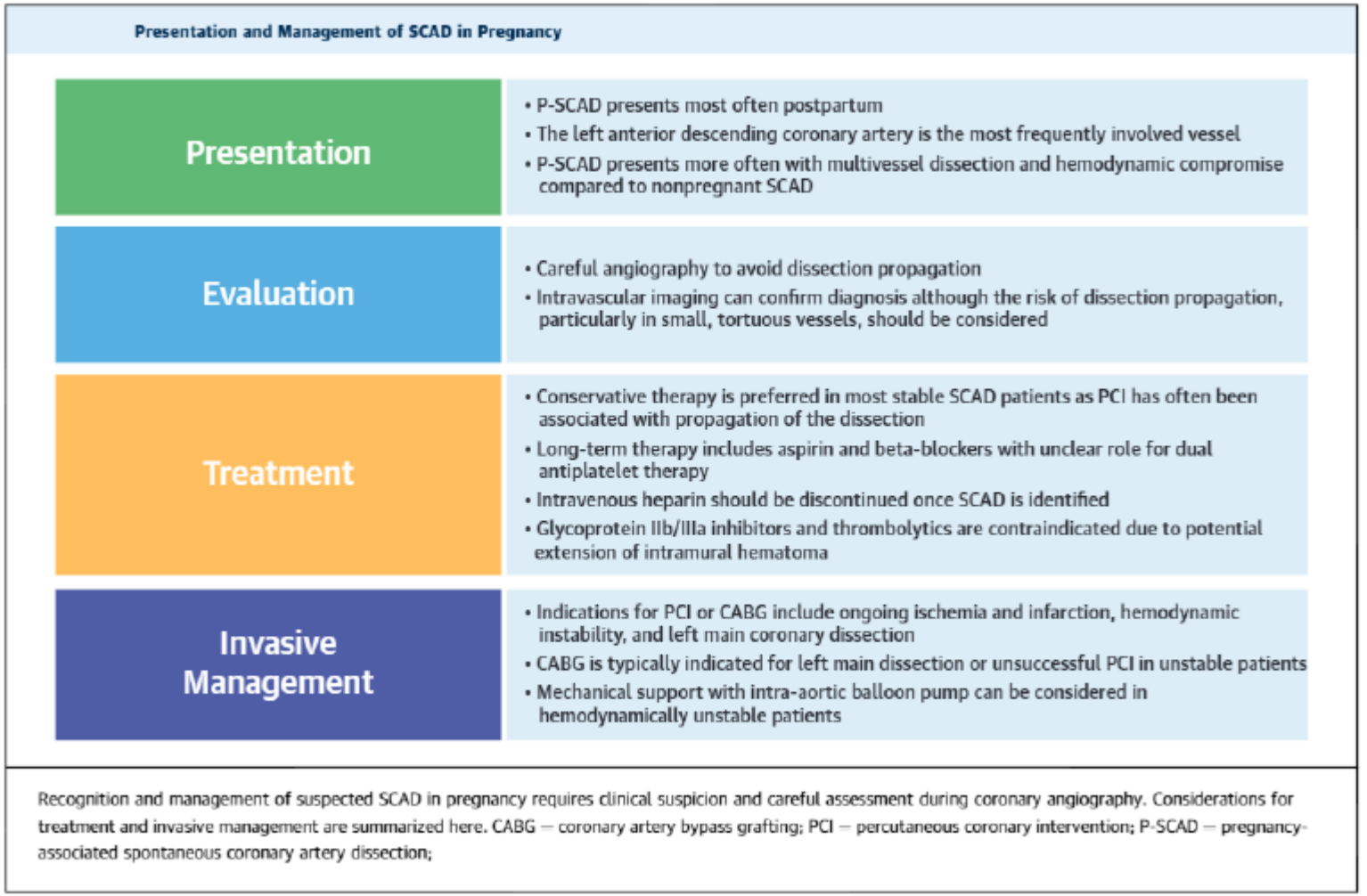

Recognition and management of suspected SCAD in pregnancy requires clinical suspicion and careful assessment during coronary angiography. Considerations for treatment and invasive management are summarized here. CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention; P-SCAD = pregnancy-associated spontaneous coronary artery dissection;

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Table 12 Management of coronary artery disease

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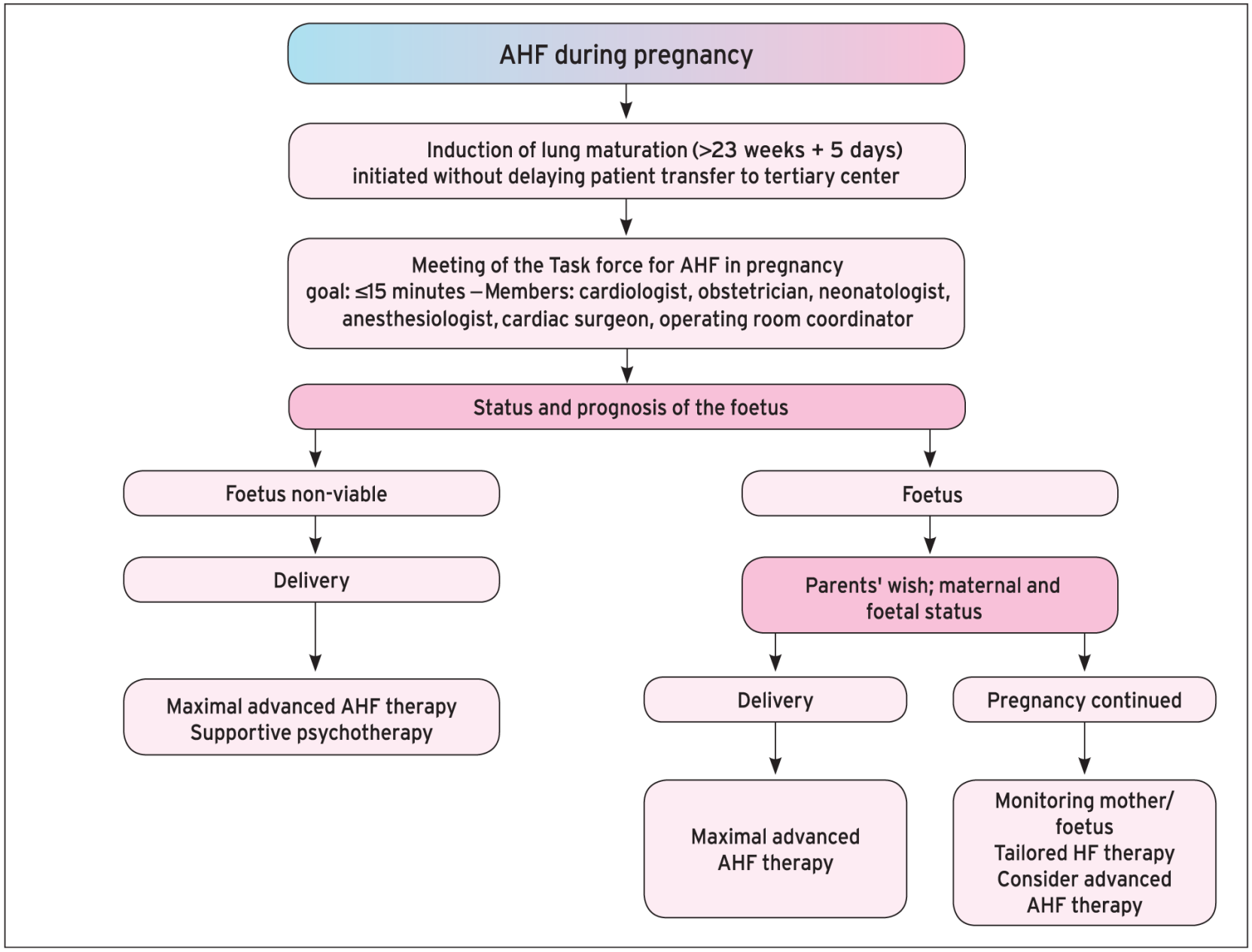
Recommendations	Class	Level
ECG and measurement of troponin levels are recommended when a pregnant woman has chest pain.	I	C
Primary coronary angioplasty is recommended as the preferred reperfusion therapy for STEMI during pregnancy.	I	C
An invasive management strategy should be considered for NSTE-ACS with risk criteria.	IIa	C
Conservative management should be considered for stable NSTEMI/NSTE-ACS with low risk criteria.	IIa	C
Follow-up should be considered over at least the next 3 months.	IIa	C
Breastfeeding is not recommended in mothers who take antiplatelet agents other than low-dose aspirin due to a lack of data.	III	C


AHF during pregnancy
Induction of lung maturation (>23 weeks + 5 days) initiated without delaying patient transfer to tertiary center
Meeting of the Task force for AHF in pregnancy goal: ≤15 minutes – Members: cardiologist, obstetrician, neonatologist, anesthesiologist, cardiac surgeon, operating room coordinator
Status and prognosis of the foetus
Foetus non-viable
Delivery
Maximal advanced AHF therapy Supportive psychotherapy
Foetus
Parents' wish; maternal and foetal status
Delivery
Maximal advanced AHF therapy
Pregnancy continued
Monitoring mother/ foetus Tailored HF therapy Consider advanced AHF therapy
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Management of acute heart failure

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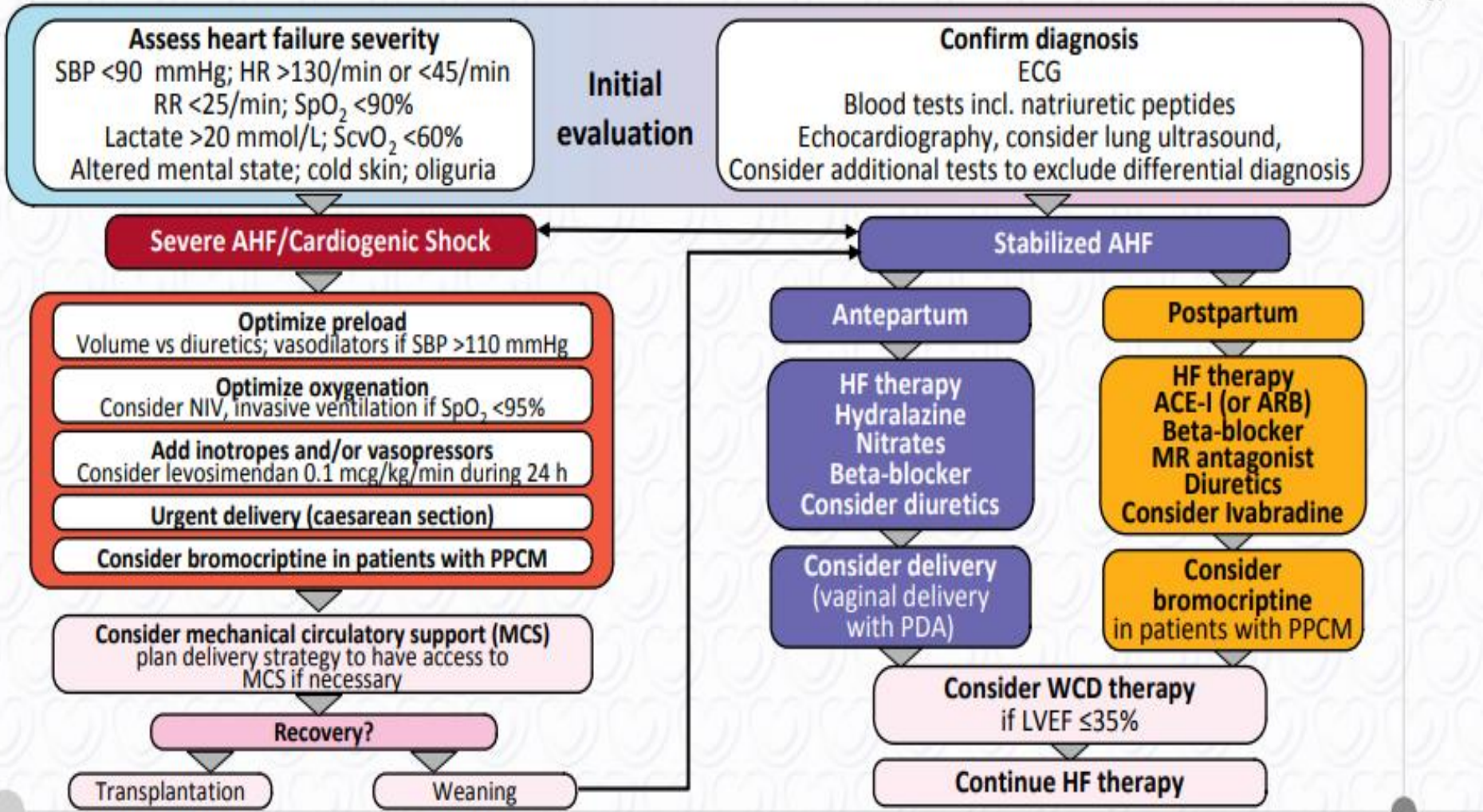

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Management of cardiomyopathies and heart failure
Selected recommendations

Recommendations	Class	Level
Anticoagulation is recommended in patients with intracardiac thrombus detected by imaging or with evidence of systemic embolism.	I	A
It is recommended to treat women with HF during pregnancy according to current guidelines for non-pregnant patients, respecting contraindications for some drugs in pregnancy (see Table 19).	I	B
Bromocriptine treatment should be accompanied by prophylactic (or therapeutic) anticoagulation.	IIa	C
Due to the high metabolic demands of lactation and breastfeeding, preventing lactation may be considered in patients with severe HF.	IIb	B
In patients with PPCM, bromocriptine treatment may be considered to stop lactation and enhance recovery (LV fuction).	IIb	B
In women with PPCM and DCM, subsequent pregnancy is not recommended if LVEF does not normalize.	III	C

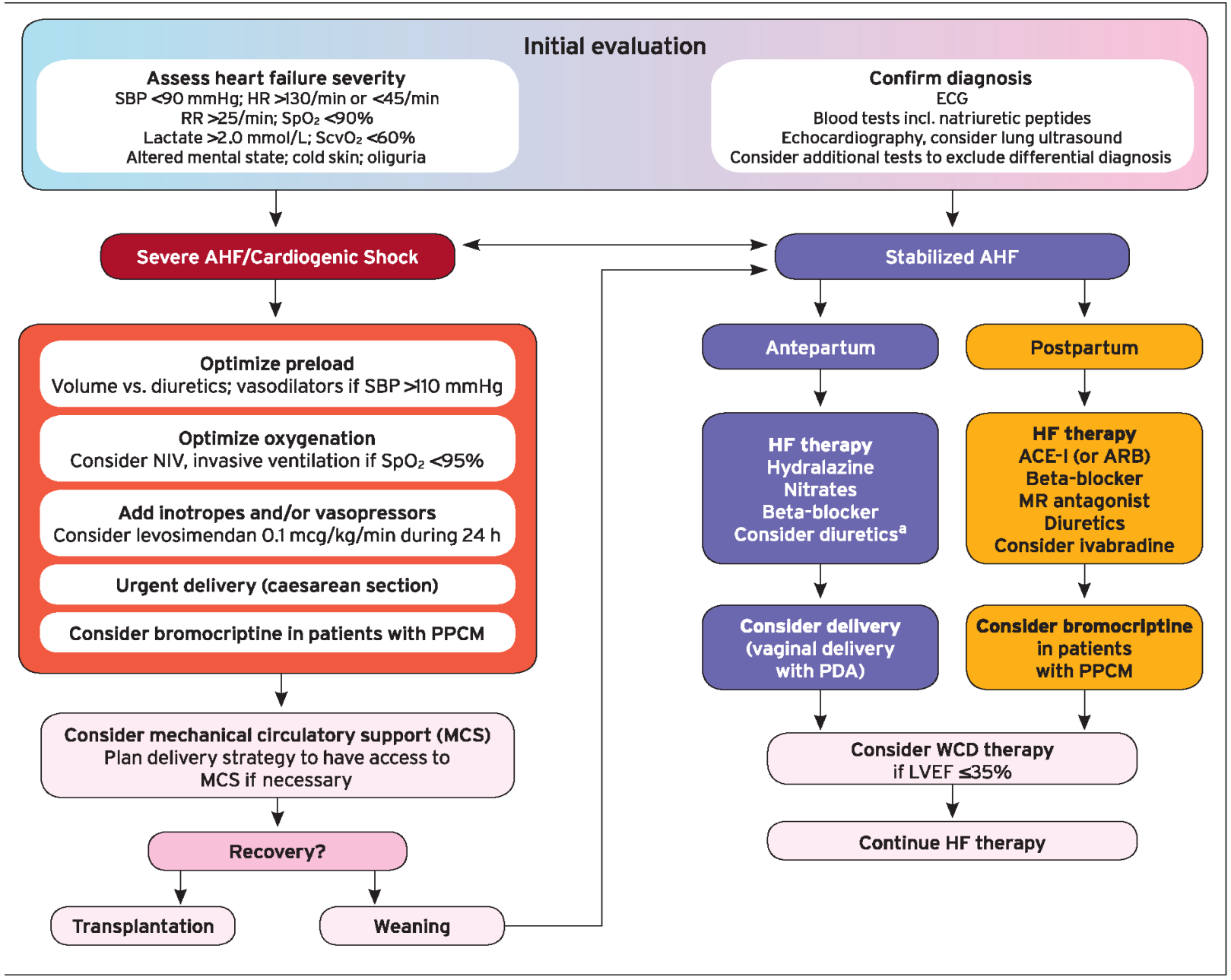
Initial evaluation
Assess heart failure severity
SBP <90 mmHg; HR >130/min or <45/min
RR >25/min; SpO2 <90%
Lactate >2.0 mmol/L; ScvO2 <60%
Altered mental state; cold skin; oliguria
Confirm diagnosis
ECG
Blood tests incl. natriuretic peptides
Echocardiography, consider lung ultrasound
Consider additional tests to exclude differential diagnosis
Severe AHF/Cardiogenic Shock
Stabilized AHF
Optimize preload
Volume vs. diuretics; vasodilators if SBP >110 mmHg
Optimize oxygenation
Consider NIV, invasive ventilation if SpO2 <95%
Add inotropes and/or vasopressors
Consider levosimendan 0.1 mcg/kg/min during 24 h
Urgent delivery (caesarean section)
Consider bromocriptine in patients with PPCM
Consider mechanical circulatory support (MCS)
Plan delivery strategy to have access to MCS if necessary
Recovery?
Transplantation
Weaning
Antepartum
Postpartum
HF therapy
Hydralazine
Nitrates
Beta-blocker
Consider diuretics[a]
HF therapy
ACE-I (or ARB)
Beta-blocker
MR antagonist
Diuretics
Consider ivabradine
Consider delivery (vaginal delivery with PDA)
Consider bromocriptine in patients with PPCM
Consider WCD therapy
if LVEF ≤35%
Continue HF therapy
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Figure 5 Management of acute heart failure during pregnancy: rapid interdisciplinary workup and treatment of mother and foetus

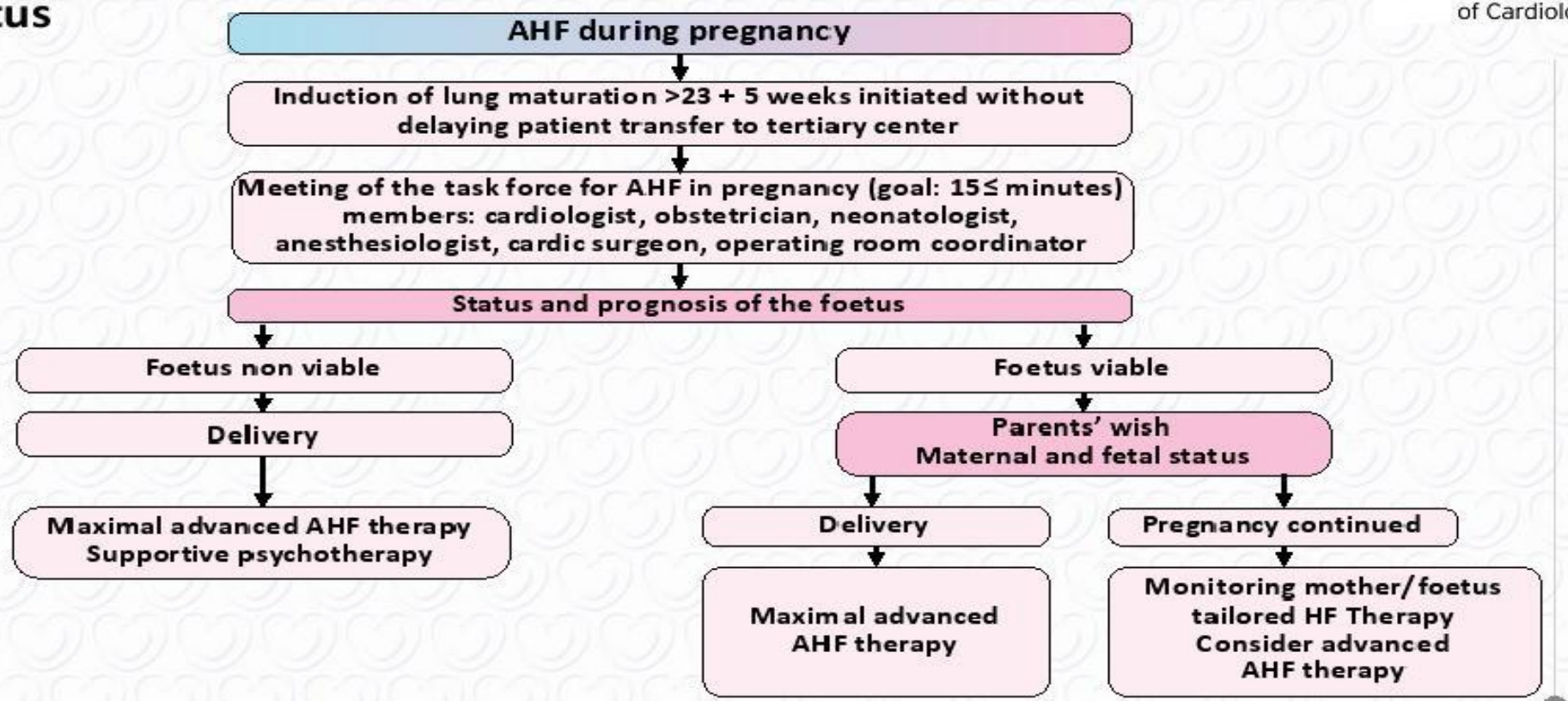

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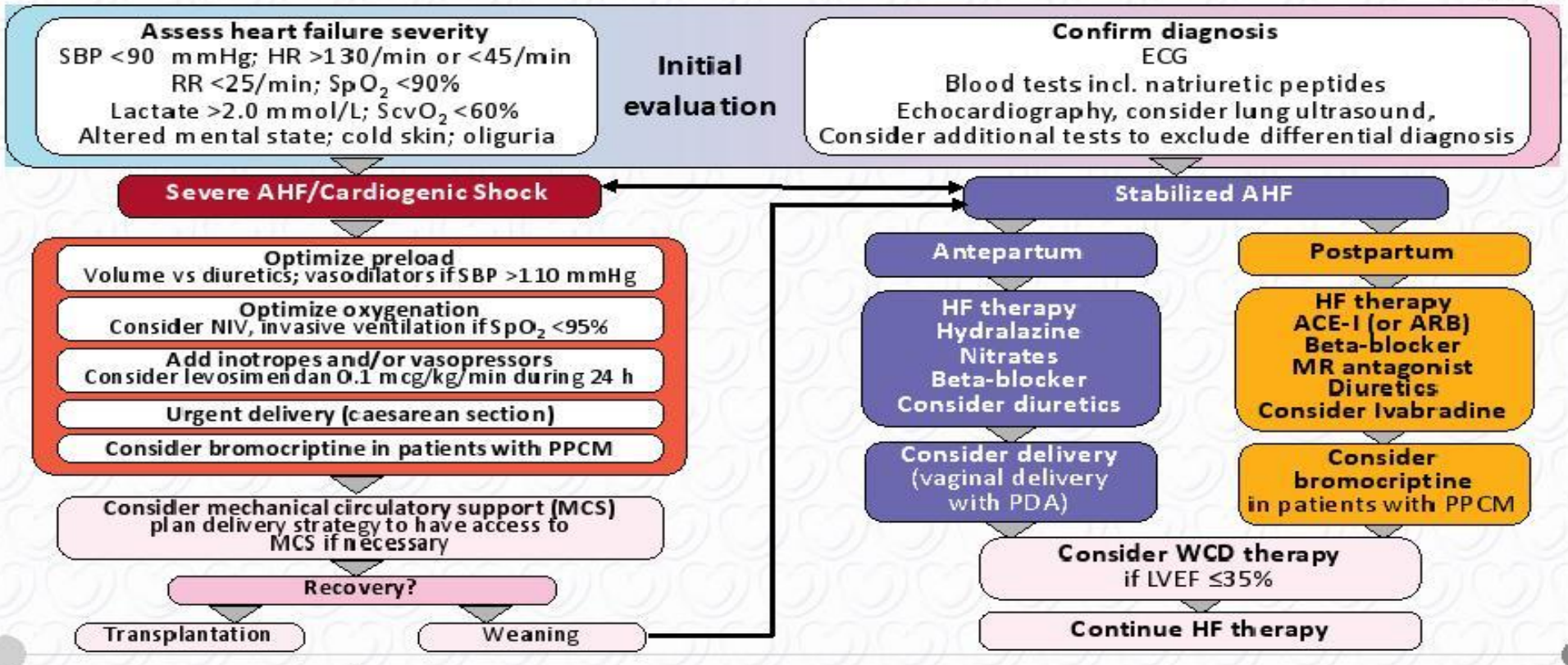
Figure 6 Management of acute heart failure during/after pregnancy



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Cardiomyopathies

- Peripartum cardiomyopathy (PPCM), toxic, hypertrophic (HCM), dilated (DCM), Tako-tsubo cardiomyopathy (TTC), and storage diseases are rare, but may cause severe complications in pregnancy.
- **PPCM** presents with HF secondary to LV systolic dysfunction towards the end of pregnancy and in the months following delivery. The EF is usually < 45 %, mortality ranges from 2.0% in Germany to 24 % in Turkey.
- **Management goals** are similar to non-pregnant acute HF, while **avoiding fetotoxic agents** (ACE inhibitors, ARB, ARNI, MRA).
- **Bromocriptine** is emerging as a new concept, always with anticoagulation
- In women with PPCM and DCM, there is a major risk for **deterioration** in a subsequent pregnancy, if LVEF does not normalize.

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Cardiomyopathies
Peripartum Cardiomyopathy

Multiple Pregnancy

Afro-Caribbean Race

Pregnancy complicated by Hypertension

Advanced maternal age

Multiparity

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Cardiomyopathies
Peripartum Cardiomyopathy

- New-onset left ventricular dysfunction without other cause, occurring at the end of pregnancy or following delivery.
- Non-specific presentation and medical therapy (excluding ACE-inhibitors) (IB).
- Spontaneous recovery in half of cases.
- Risk of recurrence during subsequent pregnancies, even after recovery of left ventricular function.

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Cardiomyopathies
Peripartum Cardiomyopathy

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- Non-specific presentation and medical therapy (excluding ACE-inhibitors) (IB).
- Spontaneous recovery in half of cases.
- Risk of recurrence during subsequent pregnancies, even after recovery of left ventricular function.

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Peripartum cardiomyopathy (PPCM)

- HF can develop rapidly, use guidelines for acute and chronic HF, consider contraindications for some drugs (I).
- Spontaneous recovery can occur (up to 50%).
- Avoid ACEI, ARB and renin inhibitors, if possible. Prefer hydralazine and nitrates, dopamine, levosimenden, digitalis; ß1 selective blockers; use diuretics with caution.
- Use anticoagulation with LMWH or OAC according to pregnancy state in pts with intracardiac thrombi, embolisms, atrial fibrillation (I).
- Deterioration in LV function occurs in up to 50% and carries a poor prognosis.

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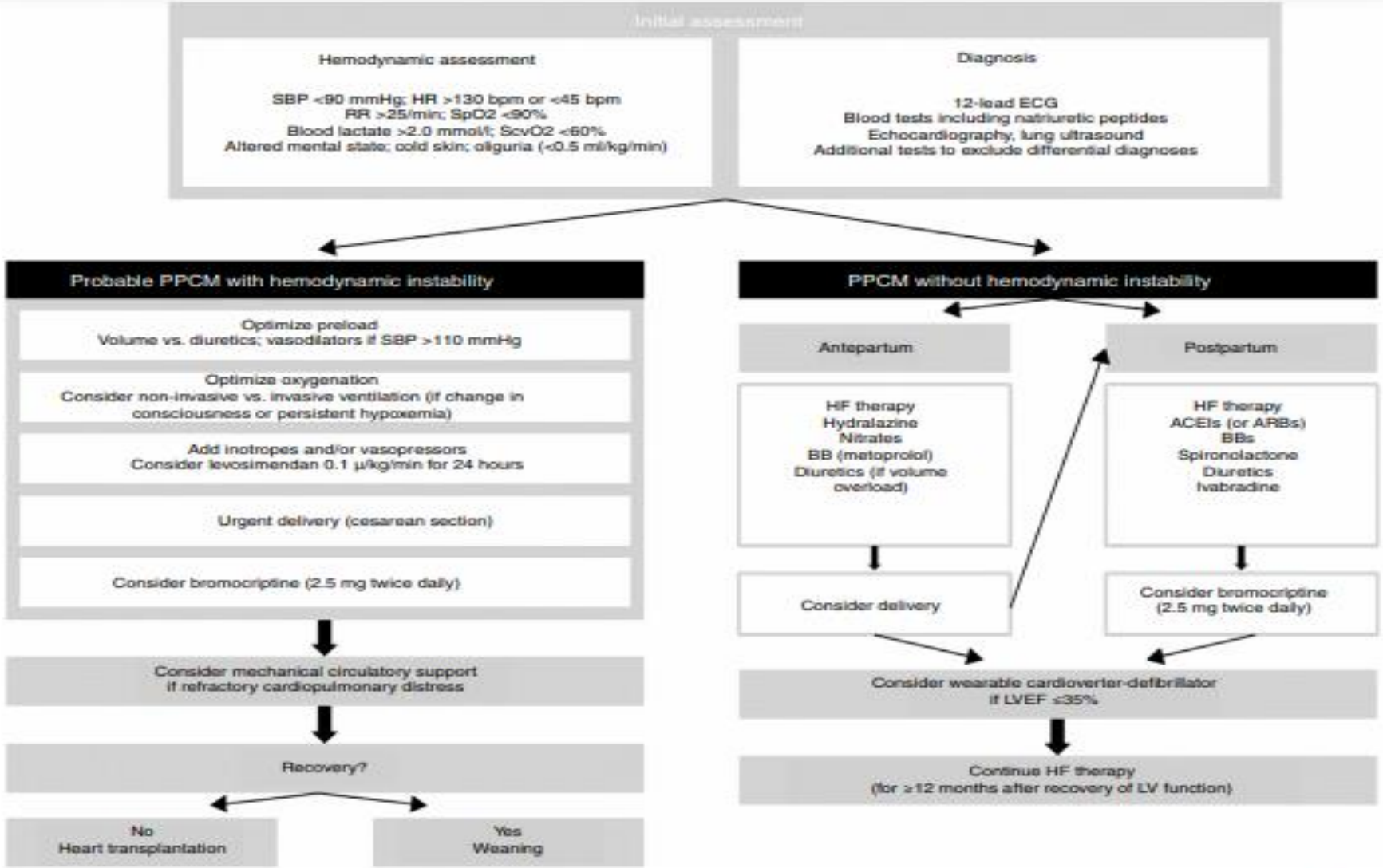

Figure 1 Algorithm for management of patients with peripartum cardiomyopathy (adapted from Bauersachs et al.[12]). ACEIs: angiotensin-converting enzyme inhibitors; ARBs: angiotensin receptor blockers; BBs: beta-blockers; ECG: electrocardiogram; HF: heart failure; HR: heart rate; IV: invasive ventilation; LV: left ventricular; LVEF: left ventricular ejection fraction; PPCM: peripartum cardiomyopathy; RR: respiratory rate; SBP: systolic blood pressure; SpO_2: peripheral oxygen saturation; $SvcO_2$: central venous oxygen saturation.

Other Cardiomyopathies

- Dilated cardiomyopathy:
  - left ventricular dysfunction pre-exists or is revealed at the beginning of pregnancy,
  - high risk if left ventricular ejection fraction <
  - treatment as in PPCM,
  - women with DCM should be informed about the risk of deterioration during gestation and peripartum,
  - LVEF < 40% is a predictor of high risk. If LVEF is < 20%, maternal mortality is very high and termination of the pregnancy should be considered.

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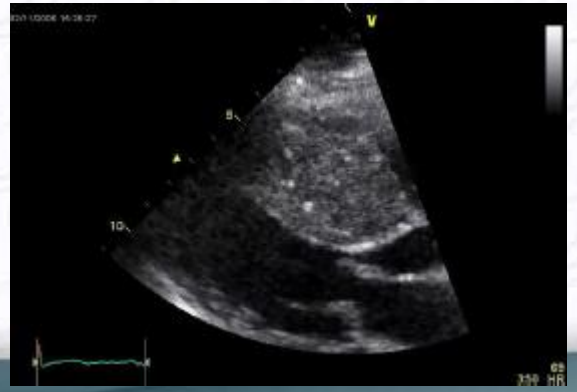
Other Cardiomyopathies

- Hypertrophic cardiomyopathy:
  - low risk if previously well tolerated,
  - severity of LVOTO determines risk during pregnancy and delivery,
  - beta-blockers indicated according to hypertrophy and gradient (IIaC),
  - treat AF, use LMWH or OAC if AF occurs.



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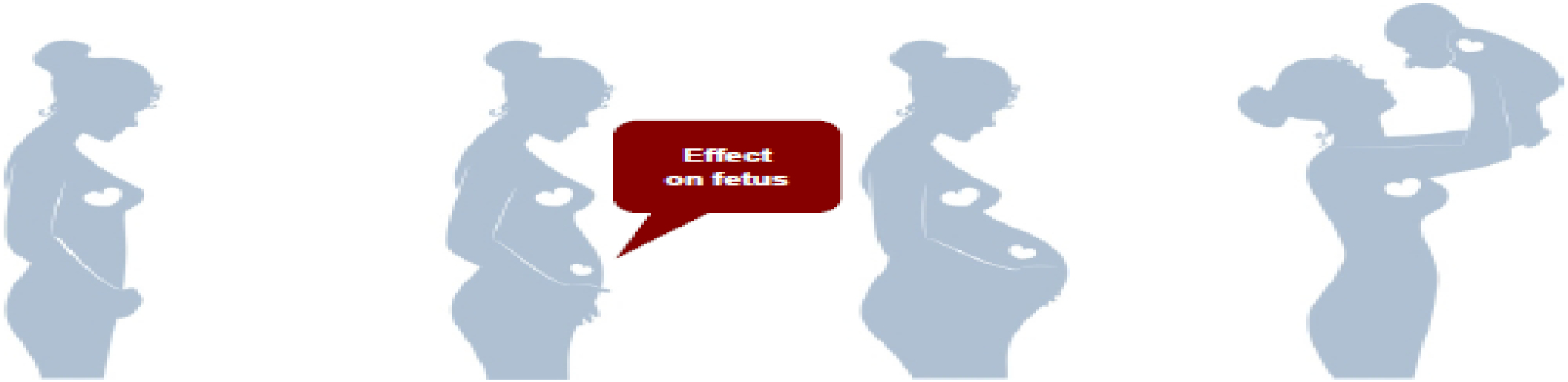
Other Cardiomyopathies

Medical Treatment of Heart Failure in peripartum women



Non Pregnant (cardiomyopathy)	Early Pregnancy	Late Pregnancy	Postpartum
According to standard heart failure guidelines	Diuretics Hydralazine Beta Blocker	Diuretics Hydralazine Beta Blocker	Diuretics Ace-inhibitor Beta blocker

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Table 13 Management of cardiomyopathies and heart failure (1)

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Recommendations	Class	Level
Anticoagulation is recommended in patients with intracardiac thrombus detected by imaging or with evidence of systemic embolism.	I	A
It is recommended to treat women with HF during pregnancy according to current guidelines for non-pregnant patients, respecting contraindications for some drugs in pregnancy (see Table 19).	I	B
It is recommended to inform women with HFrEF about the risk of deterioration of the condition during gestation and peripartum.	I	C
Therapeutic anticoagulation with LMWH or vitamin K antagonists according to the stage of pregnancy is recommended for patients with atrial fibrillation.	I	C
In HFrEF, it is recommended that beta-blockers are continued in women who used them before pregnancy or are installed with caution, if symptoms persist.	I	C
In patients with PPCM and DCM, counselling for recurrence risk during subsequent pregnancy is recommended in all cases, even after recovery of LV function.	I	C

Table 13 Management of cardiomyopathies and heart failure (2)

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Recommendations	Class	Level
As rapid diagnosis and decision-making is crucial for all pregnant women with acute HF, a pre-specified management algorithm and an interdisciplinary team should be established.	IIa	C
Patients in cardiogenic shock/dependent on inotropes should be transferred early to a facility where mechanical circulatory support is available.	IIa	C
Bromocriptine treatment should be accompanied by prophylactic (or therapeutic) anticoagulation.	IIa	C
Due to the high metabolic demands of lactation and breastfeeding, preventing lactation may be considered in patients with severe HF.	IIb	B
In patients with PPCM, bromocriptine treatment may be considered to stop lactation and enhance recovery (LV fuction).	IIb	B
In women with PPCM and DCM, subsequent pregnancy is not recommended if LVEF does not normalize.	III	C

Table 13 Management of cardiomyopathies and heart failure (3)

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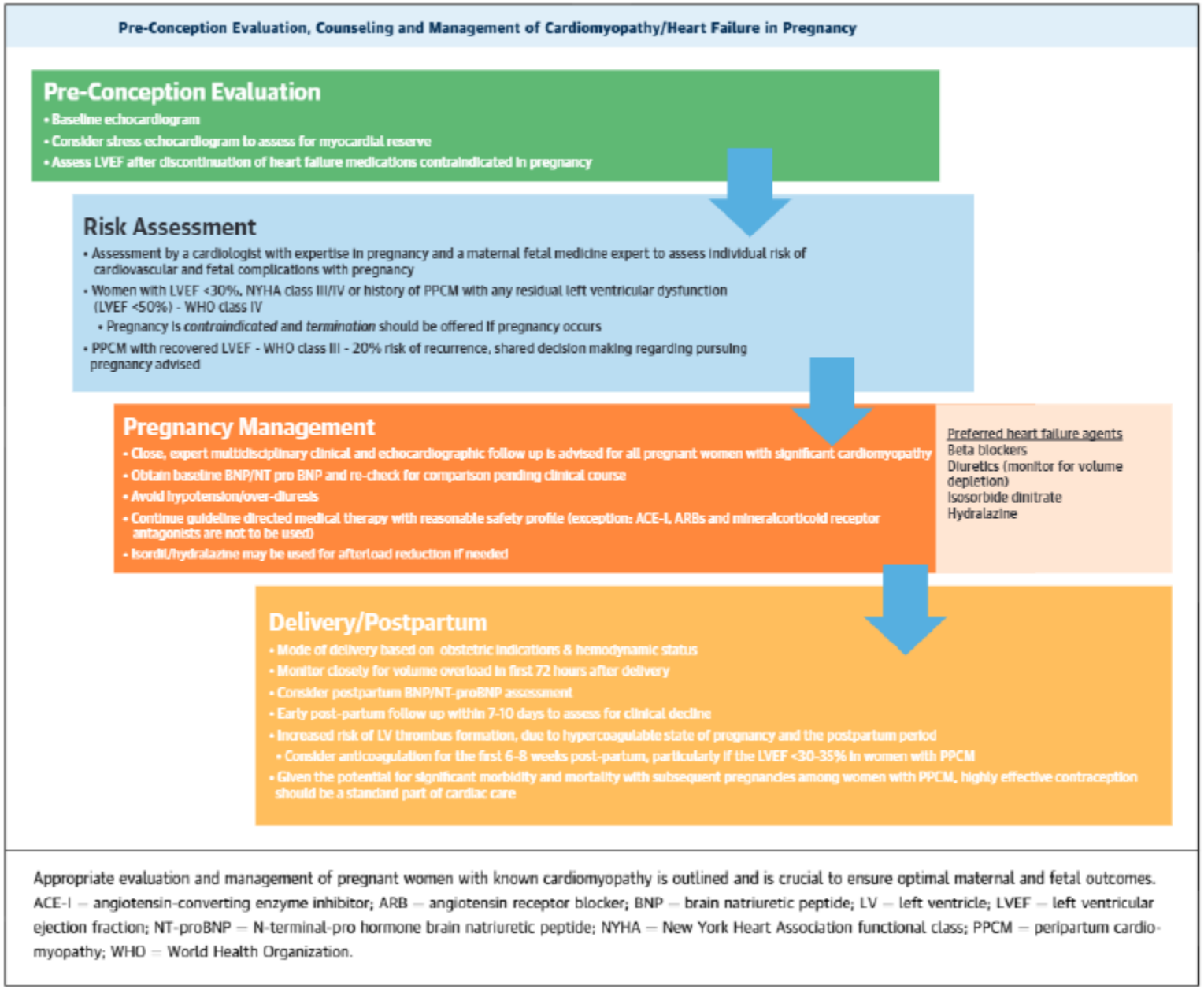
Recommendations	Class	Level
HCM		
In patients with HCM, the same risk stratifications as for non-pregnant women are recommended.	I	C
In patients with HCM, it is recommended that beta-blockers are continued in women who used them before pregnancy.	I	C
In patients with HCM, beta-blockers should be started in women who develop symptoms due to outflow tract obstruction or arrhythmia during pregnancy.	IIa	C
In HCM, cardioversion should be considered for persistent atrial fibrillation.	IIa	C



Appropriate evaluation and management of pregnant women with known cardiomyopathy is outlined and is crucial to ensure optimal maternal and fetal outcomes. ACE-I = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; BNP = brain natriuretic peptide; LV = left ventricle; LVEF = left ventricular ejection fraction; NT-proBNP = N-terminal-pro hormone brain natriuretic peptide; NYHA = New York Heart Association functional class; PPCM = peripartum cardiomyopathy; WHO = World Health Organization.

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Management of Hypertrophic Cardiomyopathy in Pregnancy

Medications

Beta-blockers should be continued during pregnancy or initiated if new symptoms develop.

Calcium-channel blockers including diltiazem and verapamil may be initiated if clinically indicated.

Disopyramide should only be used if the benefits clearly outweigh risks, as it may contribute to uterine contractions.

Evaluation and management

Multidisciplinary clinical and echocardiographic follow-up is recommended once per trimester.

Low blood pressure should be promptly evaluated with echocardiography to assess for left ventricular outflow tract obstruction.

Delivery and postpartum

Vaginal delivery with consideration of an assisted second stage is appropriate for most patients, absent an obstetric indication for cesarean delivery.

Single-shot spinal anesthesia should be avoided due to the risk of systemic hypotension; slow-dosed epidural or combined spinal-epidural anesthesia is preferred.

Patients should be monitored closely postpartum for evidence of volume depletion (e.g., due to blood loss), which can precipitate or worsen left ventricular outflow tract obstruction, and for volume overload.

Continue beta-blockade or diltiazem/verapamil through delivery and postpartum.

Ki Park et al. *J Am Coll Cardiol* 2021; 77:1799-1812

Arrhythmia

- Arrhythmias requiring treatment develop in up to 15% of the patients with structural and congenital heart disease.
- In haemodynamically unstable patients with tachycardias direct cardioversion should be considered.
- Atrial flutter and atrial fibrillation are rare, prefer cardioversion after anticoagulation.
- Life-threatening ventricular arrhythmias during pregnancy are rare.

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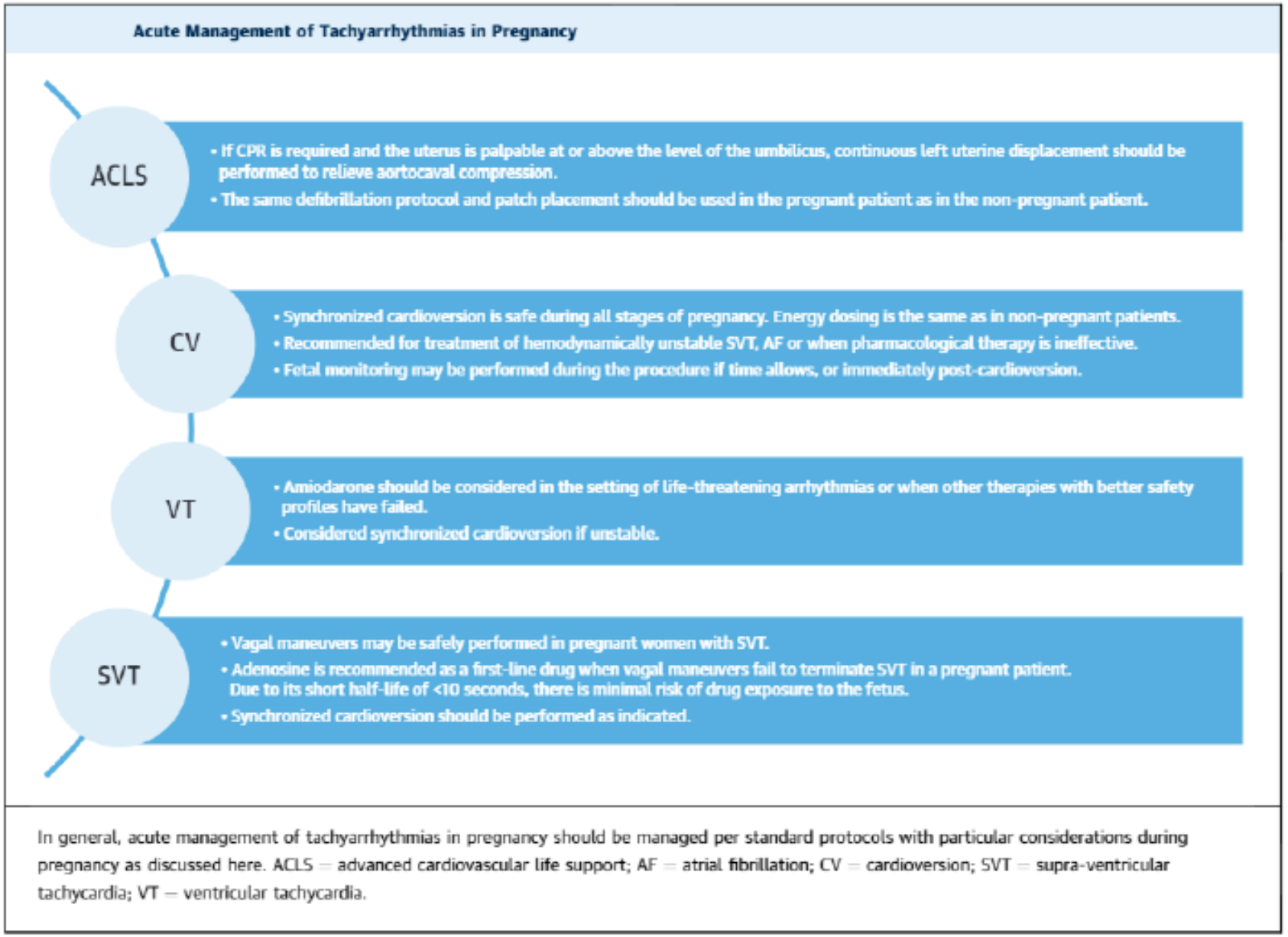

In general, acute management of tachyarrhythmias in pregnancy should be managed per standard protocols with particular considerations during pregnancy as discussed here. ACLS = advanced cardiovascular life support; AF = atrial fibrillation; CV = cardioversion; SVT = supra-ventricular tachycardia; VT = ventricular tachycardia.

Ki Park et al. *J Am Coll Cardiol* 2021; 77:1799-1812

Drugs	Classification (Vaughan Williams for AA drugs)	FDA category	Placenta permeable	Transfer to breast milk (fetal dose)	Adverse effects
Adenosine	Antiarrhythmic	C	No	No	No fetal adverse effects reported (limited human data)
Amiodarone	Class III	D	Yes	Yes	Thyroid insufficiency (9%), hyperthyroidism, goitre, bradycardia, growth retardation, premature birth
Atenolol	Class II	D	Yes	Yes	Hypospadias (first trimester); birth defects, low birth weight, bradycardia and hypoglycemia in fetus
Digoxin	Cardiac glycoside	C	Yes	Yes	Serum levels unreliable, safe
Diltiazem	Class IV	C	No	Yes	Possible teratogenic effects.

European Heart J 2011;32:3147-3197 Heart 2007;93::1630-36 Current Opinion in Cardiol 2001;16:40-

Drugs	Classification (Vaughan Williams for AA drugs)	FDA category	Placenta permeable	Transfer to breast milk (fetal dose)	Adverse effects
Disopyramide	Class IA	C	Yes	Yes	Uterus contraction
Flecainide	Class IC	C	Yes	Yes	Unknown (limited experience)
Lidocaine	Class IB	B	Yes	Yes	Fetal bradycardia, acidosis, central nervous system toxicity
Metoprolol	Class II	C	Yes	Yes	Bradycardia and hypoglycemia in fetus
Mexiletine	Class IB	C	Yes	Yes	Fetal bradycardia
Procainamide	Class IA	C	Yes	Yes	Unknown (limited experience)
Propafenone	Class IC	C	Yes	Unknown	Unknown (limited experience)
Propranolol	Class II	C	Yes	Yes	Bradycardia and hypoglycemia in fetus

European Heart J 2011;32:3147-3197 Heart 2007;93::1630-36 Current Opinion in Cardiol 2001;16:40-45

Drugs	Classification (Vaughan Williams for AA drugs)	FDA category	Placenta permeable	Transfer to breast milk (fetal dose)	Adverse effects
Quinidine	Class IA	C	Yes	Yes	Thrombopenia, premature birth, VIII th nerve toxicity.
Sotalol	Class III	B	Yes	Yes	Bradycardia and hypoglycemia in fetus (limited experience)
Verapamil oral	Class IV	C	Yes	Yes	Well tolerated (limited experience during pregnancy)
Verapamil i.v.	Class IV	C	Yes	Yes	Intravenously use is may be associated with a greater risk of hypotension and subsequent fetal hypoperfusion
Vernakalant	Class III	-	Unknown	Unknown	No experience of use in pregnancy.

European Heart J 2011;32:3147-3197 Heart 2007;93::1630-36 Current Opinion in Cardiol 2001;16:40–45

Table 14 Surveillance levels at time of delivery in women with arrhythmias (1)

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Risk for arrhythmia with Haemodynamic compromise at delivery		Level of Surveillance [a]	Class[b]	Level[c]
Low risk	PSVT, AF, idiopathic VT, low-risk LQTS, WPW syndrome	1	I	C
Medium risk	Unstable SVT, VT, ICD carriers, VT and structural heart disease, Brugada syndrome; moderate risk: LQTS, catecholaminergic polymorphic VT	2	I	C
High risk for life threatening arrhythmia	Unstable VT in structural heart disease/congenital heart disease, unstable VT/TdP in high-risk LQTS patients, short QT syndrome, high-risk catecholaminergic polymorphic VT	3	I	C

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Table 14 Surveillance levels at time of delivery in women with arrhythmias (2)

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Descriptions of actions to be planned	Surveillance level		
	Low 1	Medium 2	High 3
Consult cardiologist	x		
Consultation with multidisciplinary team including arrhythmologists at specialized centre		x	x
Mode and location of delivery as advised by obstetricians	x	x	
Caesarean delivery recommended			x
Monitor cardiac rhythm (telemetry, external rhythm monitor)		(x)	x
Intravenous line		x	x
Arterial line			x

Table 14 Surveillance levels at time of delivery in women with arrhythmias (3)

ESC European Society of Cardiology

Descriptions of actions to be planned	Surveillance level		
	Low 1	Medium 2	High 3
Prepare for intravenous administration of adenosine		x	
Prepare for intravenous administration of a beta-blocker		x	x
Prepare for intravenous administration of selected antiarrhythmic drugs			x
External cardioverter defibrillator at site		x	x
Delivery at thoracic operating theatre			x
Prepare for transfer to cardiac intensive care unit post-partum if needed			x

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Table 15 Management of arrhythmias (1)

ESC European Society of Cardiology

Recommendations	Class	Level
Acute management (intravenous administration of drugs) of SVT and AF		
Vagal manoeuvres, followed by adenosine if these fail, are recommended for acute conversion of PSVT.	I	C
Immediate electrical cardioversion is recommended for any tachycardia with haemodynamic instability and for pre-excited AF.	I	C
Beta-1-selective blockers should be considered for acute conversion of PSVT.	IIa	C
Ibutilide or flecainide may be considered for termination of atrial flutter and AF in stable patients with structurally normal hearts.[c]	IIb	C
Long-term management (oral administration of drugs) of SVT and AF		
Beta-1-selective blockers or verapamil is recommended for the prevention of SVT in patients without pre-excitation on resting ECG.	I	C
Flecainide[e] or propafenone[e] are recommended for the prevention of SVT in patients with WPW syndrome.	I	C

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Table 15 Management of arrhythmias (2)

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Recommendations	Class	Level
Long-term management (oral administration of drugs) of SVT and AF *(cont'd)*		
Beta-selective blockers are recommended for rate control of AT or AF.	I	C
Flecainide[e], propafenone,[e] or sotalol[f] should be considered to prevent SVT, AT, and AF if AV nodal blocking agents fail.	IIa	C
Digoxin and verapamil should be considered for rate control of AT or AF if beta-blockers fail.	IIa	C
Catheter ablation with electroanatomical systems should be considered in experienced centres in cases of drug-refractory and poorly tolerated SVT.	IIa	C
Acute management (intravenous administration of drugs) of ventricular tachyarrhythmias		
Immediate electrical cardioversion is recommended for sustained both unstable and stable VT.	I	C
For acute conversion of sustained, haemodynamically stable, monomorphic VT (e.g. idiopathic VT), a beta-blocker, sotalol,[f] flecainide,[e] procainamide, or overdrive ventricular pacing should be considered.	IIa	C

Table 15 Management of arrhythmias (3)

ESC European Society of Cardiology

Recommendations	Class	Level
Long-term management (oral administration of drugs) of Ventricular tachyarrhythmias		
ICD (preferably one chamber) is recommended prior to pregnancy if clinically indicated but also during pregnancy, preferably using echocardiographic guidance or mapping, especially if the foetus is beyond 8 weeks of gestation, if indication emerges.	I	C
Beta-blocking agents are recommended during pregnancy and post-partum in patients with long QT syndrome or catecholaminergic polymorphic VT.	I	C
Beta-blocking agents or verapamild,e are recommended for the prevention of idiopathic sustained VT if associated with severe symptoms or haemodynamic compromise.	I	C
In idiopathic sustained VT, sotalol[f] or flecainide[e] should be considered for prevention if other drugs fail.	IIa	C
Catheter ablation with electroanatomical mapping systems may be considered in experienced centres in sustained drug-refractory and poorly tolerated VT if there are no other alternatives.	IIb	C

Venous Thromboembolism

- Assessment of risk factors for venous thromboembolism is recommended in all pregnant women (IC).
- Antenatal and postpartum (6 weeks) prophylaxis with LMWH:
  - is recommended in high-risk patients (IC),
  - should be considered in intermediate-risk patients (IIaC).
- D-dimer measurement and compression ultrasonography is recommended in patients with suspected venous thromboembolism (IC).
- CT pulmonary angiography is favoured for the diagnosis of pulmonary embolism.

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Check list - risk factors for venous thromboembolism

Pre-existing risk factors
Previous recurrent VTE.
Previous VTE-unprovoked or oestrogen related.
Previous VTE-provoked.
Family history of VTE.
Known thrombophilia.
Medical co-morbidities, e.g. heart or lung diseases, SLE, cancer, inflammatory conditions, nephritic syndrome, sickle cell disease, i.v. drug use.
Age > 35 years.
Obesity, BMI >30 kg/m^2.
Parity ≥ 3.
Smoker.
Gross varicous veins.

Obstetric risk factors
Pre-eclampsia.
Dyhydration/hyperemesis/ovarian hyperstimulation syndrome.
Multiple pregnancy or assisted reproductive therapy.
Emergency caesarean section.
Elective caesarean section.
Mid-cavity or rotational forceps.
Prolonged labour (> 24 hours).
Peripartum haemorrhage (> 1 L or transfusion).
Transient risk factors
Current systemic infection.
Immobility.
Surgical procedure in pregnancy or < 6 weeks post-partum.

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Recommendations for the management of venous thromboembolism

Recommendations	Class	Level
In all women who are pregnant or consider pregnancy, assessment of risk factors for VTE is recommended.	I	C
Mothers should be informed about the signs and symptoms of VTE in pregnancy and the necessity to contact the physicians if they occur.	I	C
High risk patients should receive antenatal prophylaxis with LMWH as well as post-partum for the duration of 6 weeks.	I	C
In intermediate risk patients post-partum prophylaxis with LMWH should be given for at least 7 days or longer, if ≥ 3 risk factors persist.	I	C
In low risk patients early mobilization and avoidance of dehydration is recommended.	I	C
Graduated compression stockings are recommended antepartum and post-partum in all women at high risk.	I	C
D-Dimer measurement and compression ultrasonography is recommended in patients with suspected VTE during pregnancy.	I	C
For treatment of acute VTE during pregnancy, UFH is recommended in high-risk and LMWH in non-high risk patients.	I	C

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Recommendations for the management of venous thromboembolism

Recommendations	Class	Level
Graduated compression stockings should be considered in women with intermediate risk during pregnancy and post-partum.	IIa	C
In intermediate risk patients, antenatal prophylaxis with LMWH should be considered.	IIa	C
Routine screening for thrombophilia should not be performed.	III	C

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Table 17 Prevention and treatment of venous thrombo-embolism (1)

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Recommendations	Class	Level
LMWH is recommended for the prevention and treatment of VTE in pregnant patients.	I	B
For high-risk women, it is recommended to give a weight-related prophylactic dose of LMWH (e.g. enoxaparin 0.5 mg/kg once daily)	I	B
A documented assessment of risk factors for VTE before pregnancy or in early pregnancy is recommended in all women.	I	C
It is recommended that the therapeutic dose of LMWH is based on body weight.	I	C
Thrombolytics to manage patients with pulmonary embolism is only recommended in patients with severe hypotension or shock.	I	C
In high-risk women, it is recommended to convert LMWH to UFH at least 36 h prior to delivery and stop the UFH infusion 4–6 h prior to anticipated delivery. aPTT should be normal before regional anaesthesia.	I	C

Table 17 Prevention and treatment of venous thrombo-embolism (2)

ESC European Society of Cardiology

Recommendations	Class	Level
In low-risk women on therapeutic LMWH, induction or caesarean section is recommended to be performed 24 h after the last dose of LMWH.	I	C
For women after in vitro fertilization complicated by OHSS, thrombo-prophylaxis with LMWH is recommended during the first trimester.	I	C
In women who are on antenatal anticoagulation, it should be considered to actively manage the third stage of labour with Oxytocin.	IIa	C
If compression ultrasound is negative, using magnetic resonance venography should be considered to diagnose pelvic thrombosis before using computed tomography pulmonary angiography or ventilation perfusion scanning.	IIa	C
In women on therapeutic LMWH, planned delivery should be considered at around 39 weeks to avoid the risk of spontaneous labour while fully anticoagulated (LMWH is only partially reversed with protamine).	IIa	C
Direct oral anticoagulants are not recommended in pregnancy.	III	C

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Drug therapy in pregnancy

- No uniform recommendations!
- In case of emergency, drugs that are not recommended during pregnancy and breast feeding should not be withheld to the mother. The potential risk and benefit must be weighed against each other.
- Different sources of evidence such as U.S. Food and Drug Administration (FDA) classification, Internet databases, Pharmaceutical industry recommendations have different strength and weaknesses.
- Overview table with major CV drugs/families, FDA category, placenta permeability, transfer to breast milk, adverse effects.

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Drug therapy in pregnancy

Recommendations for drug use

Drug	Classification (Vaughan Williams for AA drugs)	FDA category	Placenta permeable	Transfer to breast milk (fetal dose)	Adverse effects
Abciximab	Monoclonal antibody with antithrombotic effects	C	Unknown	Unknown	Inadequate human studies; should be given only if the potential benefit outweighs the potential risk to the fetus.
Acenocoumarol	Vitamin K antagonist	D	Yes	Yes (no adverse effects reported)	Embryopathy (mainly first trimester), bleeding (see further discussion in Section 5 for use during pregnancy).
Acetylsalicylic acid (low dose)	Antiplatelet drug	B	Yes	Well-tolerated	No teratogenic effects known (large datasets).
Adenosine	Antiarrhythmic	C	No	No	No fetal adverse effects reported (limited human data).
Aliskiren	Renin inhibitor	D	Unknown	Unknown	Unknown (limited experience).
Amiodarone	Antiarrhythmic (Class III)	D	Yes	Yes	Thyroid insufficiency (9%), hyperthyroidism, goitre, bradycardia, growth retardation, premature birth.
Ampicillin, amoxicillin, cephalosporins, erythromycin, mezlocillin, penicillin	Antibiotics	B	Yes	Yes	No fetal adverse effects reported.

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Drug therapy in pregnancy

Drug	FDA category	Placenta permeable	Tranfer to breast milk	Adverse effects
Aspirin	B	Yes	Well tolerated	No teratogenic effects Large experience
Abciximab	C	?	?	?
Clopidogrel	C	?	?	?
Ticlopidine	C	?	?	?
Prasugrel	C	?	?	?
Ticagrelor	C	?	Yes	?
Warfarin	D	Yes	Yes no adverse effect	Teratogenic. Dose dependent
UFH	B	No	No	Osteoporosis, thrombocytopenia
LMWH	B	No	No	Well tolerated. Better than UFH
Fondaparinux	C	Yes	No	?
Dabigatran	C	Yes	Yes	?
Rivaroxaban	C	Yes	?	?
Apixaban	C	Yes	?	?
Bivalirudin	B	?	?	?

Table 18 Drug use in pregnancy

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Recommendations	Class	Level
Before pharmacological treatment in pregnancy is started, it is recommended to check Table 19 for clinical safety data.	I	C
In the absence of clinical safety data, it is recommended to check the electronic drug table (www.safefetus.com) for pre-clinical safety data.	I	C
In the absence of adequate human safety data, decision-making should be based on individual drug efficacy and safety profiles, and the available animal data, and the decision must be made together with the patient.	IIa	C
Decision-making based on former FDA categories alone is no longer recommended.	III	C

Table 19 Drugs and safety data

Drugs	Classification (Vaughan Williams for antiarrhythmic drugs)	Former FDA category	Placenta permeable	Transfer to breast milk (foetal dose)	Pre-clinical/ clinical safety data
The table on drugs an safety data can be found in the Full text of the Guidelines and it is available at: www.escardio.org/guidelines and on the European Heart Journal web site (https://academic.oup.com/eurheartj/articlelookup/doi/10.1093/eurheartj/ehy340).					

‘What to do’ and ‘what not to do’ messages from the Guidelines (1)

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Recommendations	Class	Level
General recommendations		
Pre-pregnancy risk assessment and counselling is indicated in all women with known or suspected congenital or acquired cardiovascular and aortic disease.	I	C
It is recommended to treat high risk patients in specialized centres by a multidisciplinary team: the pregnancy heart team.	I	C
Echocardiography is recommended in any pregnant patient with unexplained or new cardiovascular signs or symptoms.	I	C
Vaginal delivery is recommended as first choice in most patients; for most important exceptions see below.	I	C
Prophylactic antibiotic therapy to prevent endocarditis during delivery is not recommended.	III	C

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‘What to do’ and ‘what not to do’ messages from the Guidelines (2)

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Recommendations	Class	Level
Pregnancy and pulmonary hypertension or congenital heart disease		
Right heart catheterization is recommended to confirm the diagnosis of PAH (group 1). This can be performed during pregnancy but with very strict indications, optimal timing, and shielding of the foetus.	I	C
Treatment dose LMWH is recommended in pregnant patients with chronic thrombo-embolic pulmonary hypertension.	IIa	C
Pregnancy is not recommended in patients with PAH.	III	B
Pregnancy is not recommended in patients with a systemic right ventricle and moderate or severely decreased ventricular function.		
Pregnancy is not recommended in patients after Fontan operation and any associated complication.	III	C

‘What to do’ and ‘what not to do’ messages from the Guidelines (3)

ESC European Society of Cardiology

Recommendations	Class	Level
Management of aortic disease		
All aortic diseases		
Imaging of the entire aorta (CT/MRI) is recommended before pregnancy in patients with a genetically proven aortic syndrome or known aortic disease.	I	C
When a woman with known aortic dilatation, (history of) dissection, or genetic predisposition for dissection becomes pregnant, strict blood pressure control is recommended.	I	C
Repeated echocardiographic imaging every 4–12 weeks (depending on the diagnosis and severity of dilatation) is recommended during pregnancy and 6 months post-partum in patients with ascending aorta dilatation.	I	C
It is recommended to deliver all women with aortic dilatation or (history of) aortic dissection in an experienced centre with a pregnancy heart team, where cardiothoracic surgery is available.	I	C
In patients with an ascending aorta <40 mm, vaginal delivery is recommended.	I	C

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‘What to do’ and ‘what not to do’ messages from the Guidelines (4)

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Recommendations	Class	Level
In patients with an ascending aorta <40 mm, vaginal delivery is recommended.	I	C
Specific syndromes		
Pregnancy is not recommended in patients with vascular Ehlers–Danlos syndrome.	III	C
Management of native valvular heart disease		
Mitral stenosis		
In patients with symptoms or pulmonary hypertension, restricted activities and beta-1-selective blockers are recommended.	I	B
Diuretics are recommended when congestive symptoms persist despite beta-blockers.	I	B
Intervention is recommended before pregnancy in patients with MS and valve area <1.0 cm^2.	I	C
Therapeutic anticoagulation using heparins or VKA is recommended in case of AF, left atrial thrombosis, or prior embolism.	I	C

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‘What to do’ and ‘what not to do’ messages from the Guidelines (5)

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Recommendations	Class	Level
Chronic regurgitant lesions		
Surgical treatment is recommended before pregnancy in patients with severe aortic or mitral regurgitation and symptoms, impaired ventricular function, or ventricular dilatation.	I	C
Medical therapy is recommended in pregnant women with regurgitant lesions when symptoms occur.	I	C
Management of prosthetic heart valves		
It is recommended to choose the valve prosthesis in women contemplating pregnancy in consultation with a pregnancy heart team.	I	C
It is recommended to manage pregnancy in women with mechanical valves in a centre with a pregnancy heart team.	I	C

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‘What to do’ and ‘what not to do’ messages from the Guidelines (6)

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Recommendations	Class	Level
If delivery starts while on VKA or in less than 2 weeks after discontinuation of a VKA, caesarean section is indicated.	I	C
It is recommended to discontinue VKA and start adjusted-dose intravenous UFH (aPTT ≥2 control) or adjusted-dose LMWH (see separate recommendations) at the 36th week of gestation.	I	C
It is recommended to anticipate the timing of delivery to ensure safe and effective peripartum anticoagulation.	I	C
Immediate echocardiography is indicated in women with mechanical valves presenting with dyspnoea and/or an embolic event.	I	C
During the second and third trimesters until the 36th week, VKAs are recommended in women needing a low dose.[a]	I	C

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‘What to do’ and ‘what not to do’ messages from the Guidelines (7)

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Recommendations	Class	Level
Management of coronary artery disease		
ECG and measurement of troponin levels is recommended when a pregnant woman has chest pain.	I	C
Primary coronary angioplasty is recommended as the preferred reperfusion therapy for STEMI during pregnancy.	I	C
Breastfeeding is not recommended in mothers who take antiplatelet agents other than low-dose aspirin due to a lack of data.	III	C
Management of cardiomyopathies and heart failure		
Anticoagulation is recommended in patients with intracardiac thrombus detected by imaging or with evidence of systemic embolism.	I	A

‘What to do’ and ‘what not to do’ messages from the Guidelines (8)

ESC European Society of Cardiology

Recommendations	Class	Level
It is recommended to treat women with heart failure during pregnancy according to current guidelines for non-pregnant patients, respecting contraindications for some drugs in pregnancy.	I	B
It is recommended to inform women with HFrEF about the risk of deterioration of the condition during gestation and peripartum.	I	C
Therapeutic anticoagulation with LMWH or VKAs according to stage of pregnancy is recommended for patients with AF.	I	C
In HFrEF, it is recommended that beta-blockers are continued in women who used them before pregnancy, or that they are installed with caution if symptoms persist.	I	C
In patients with PPCM and DCM, counselling for recurrence risk during subsequent pregnancy is recommended in all cases, even after recovery of LV function.	I	C

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‘What to do’ and ‘what not to do’ messages from the Guidelines (9)

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Recommendations	Class	Level
HCM		
In patients with HCM, it is recommended that beta-blockers are continued in women who used them before pregnancy.	I	C
Management of arrhythmias		
Acute management (intravenous administration of drugs) of SVT and AF		
Immediate electrical cardioversion is recommended for any tachycardia with haemodynamic instability and for pre-excited AF.	I	C
Long-term management (oral administration of drugs) of SVT and AF		
Beta-1-selective blockers or verapamil[b] are recommended for the prevention of SVT in patients without pre-excitation on resting ECG.	I	C

‘What to do’ and ‘what not to do’ messages from the Guidelines (10)

ESC European Society of Cardiology

Recommendations	Class	Level
Flecainide[c] or propafenone[c] are recommended for the prevention of SVT in patients with WPW syndrome.	I	C
Beta-1-selective blockers are recommended for rate control of AT or AF.	I	C
Acute management (intravenous administration of drugs) of ventricular tachyarrhythmias		
Immediate electrical cardioversion is recommended for both sustained unstable and stable VT.	I	C
Long-term management (oral administration of drugs) of ventricular tachyarrhythmias		
Beta-blocking agents are recommended during pregnancy and post-partum in patients with long QT syndrome or catecholaminergic polymorphic ventricular tachycardia.	I	C

‘What to do’ and ‘what not to do’ messages from the Guidelines (11)

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Recommendations	Class	Level
Management of hypertension		
Low-dose aspirin (100–150 mg daily) is recommended in women at high or moderate risk of pre-eclampsia from week 12 to week 36 -37.	I	A
In women with gestational hypertension or pre-existing hypertension super-imposed by gestational hypertension, or with hypertension and subclinical organ damage or symptoms, initiation of drug treatment is recommended at SBP >140 mmHg or DBP >90 mmHg. In all other cases, initiation of drug treatment is recommended at SBP ≥150 mmHg or DBP ≥95 mmHg.	I	C
SBP ≥170 mmHg or DBP ≥110 mmHg in a pregnant woman is an emergency, and hospitalization is recommended.	I	C

‘What to do’ and ‘what not to do’ messages from the Guidelines (12)

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Recommendations	Class	Level
Methyldopa, labetalol, and calcium antagonists are the drugs of choice for the treatment of hypertension in pregnancy.	I	C
It is recommended to expedite delivery in pre-eclampsia, and with adverse conditions such as visual disturbances or haemostatic disorders.	I	C
In severe hypertension, drug treatment with intravenous labetalol, oral methyldopa, or nifedipine is recommended.	I	C
Management of venous thrombo-embolism		
LMWH is recommended for the prevention and treatment of VTE in pregnant patients.	I	B
For high-risk women, it is recommended to give a weight-related prophylactic dose of LMWH (e.g. enoxaparin 0.5 mg/kg once daily).	I	B

‘What to do’ and ‘what not to do’ messages from the Guidelines (13)

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Recommendations	Class	Level
It is recommended that the therapeutic dose of LMWH is based on body weight.	I	C
Thrombolytics to manage patients with pulmonary embolism are only recommended in patients with severe hypotension or shock.	I	C
In high-risk women, it is recommended to convert LMWH to UFH at least 36 h prior to delivery and to stop the UFH infusion 4-6 h prior to anticipated delivery. aPTT should be normal before regional anaesthesia.	I	C
Drug use in pregnancy		
Before pharmacological treatment in pregnancy is started, it is recommended to check drugs and safety data.	I	C
In the absence of clinical safety data, it is recommended to check the supplementary data and www.safefetus.com for pre-clinical safety data.	I	C
Decision making based on former FDA categories alone is no longer recommended.	III	C

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Essential messages (1)

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- Risk estimation should be individualized depending on the underlying cardiac diagnosis, ventricular and valvular function, functional class, presence of cyanosis, PAPs, and other factors.
- Indications for intervention (surgical or catheter) in the majority of patients do not differ in women who consider pregnancy compared with other patients. There are a few exceptions, such as some degree of aortic dilatation and severe asymptomatic MS.
- In women with a moderate or high-risk of complications during pregnancy (mWHO II–III, III, and IV), pre-pregnancy counselling and management during pregnancy and around delivery should be performed in an expert centre by a multidisciplinary team: the pregnancy heart team.
- All women with congenital or other possibly genetic heart disease should be offered foetal echocardiography in weeks 19-22 of pregnancy.
- A delivery plan should be made between 20-30 weeks of pregnancy detailing induction, management of labour, delivery, and post-partum surveillance.

Essential messages (2)

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- Induction of labour should be considered at 40 weeks of gestation in all women with cardiac disease.
- Vaginal delivery is the first choice for the majority of patients.
- Indications for caesarean section are:
  - pre-term labour in patients on OACs,
  - aggressive aortic pathology,
  - acute intractable HF,
  - severe forms of PH (including Eisenmenger's syndrome).
- Pregnancy termination should be discussed if there is a high-risk of maternal morbidity or mortality, and/or of foetal abnormality.
- Pregnancy, and consequently fertility treatment, is contraindicated in women with mWHO class IV.

Essential messages (3)

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- All patients with known cardiac or aortic disease need investigations and counselling about the risks of pregnancy pre-pregnancy or before assisted reproductive therapy.
- The following patients should be counselled against pregnancy:
  - with a Fontan operation and additional comorbidities (ventricular dysfunction, arrhythmias, or valve regurgitation),
  - with PAH,
  - severe systemic ventricular dysfunction (EF <30% or NYHA class III–IV),
  - severe (re-)coarctation,
  - systemic right ventricle with moderate or severely decreased ventricular function,
  - with vascular Ehlers-Danlos,
  - with severe aortic dilatation or (history of) aortic dissection,

Essential messages (4)

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  - with severe MS (even when asymptomatic),
  - patients with severe AS who are symptomatic, or asymptomatic patients with impaired LV function or a pathological exercise test,
  - if LVEF does not normalize in women with previous PPCM.
- Women with a mechanical valve prosthesis are at high-risk of maternal morbidity (especially valve thrombosis and bleeding) and even mortality, and should be managed by a pregnancy heart team in expert centres.
- LMWH should only be used when weekly monitoring of anti-Xa levels with dose adjustment is available.
- Women with HF during pregnancy should be treated according to current guidelines for non-pregnant patients, respecting contraindications for some drugs in pregnancy (see table 'Recommendations for drug use in pregnancy'). When inotropes or more advanced treatment is necessary, transport to an expert centre is recommended.

Essential messages (5)

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- It is recommended to inform women with DCM and HFrEF about the risk of deterioration of the condition during gestation and peripartum.
- In women with PPCM and DCM, subsequent pregnancy is not recommended if LVEF does not normalize.
- Patients with congenital LQTS and catecholaminergic polymorphic VT are recommended beta-blockers during pregnancy and post-partum.
- Initiation of antihypertensive drug treatment is recommended in all women with persistent elevation of BP ≥150/95 mmHg and at values >140/90 mmHg in women with:
  - gestational hypertension (with or without proteinuria),
  - pre-existing hypertension with the superimposition of gestational hypertension,
  - hypertension with subclinical organ damage or symptoms at any time during pregnancy.

Essential messages (6)

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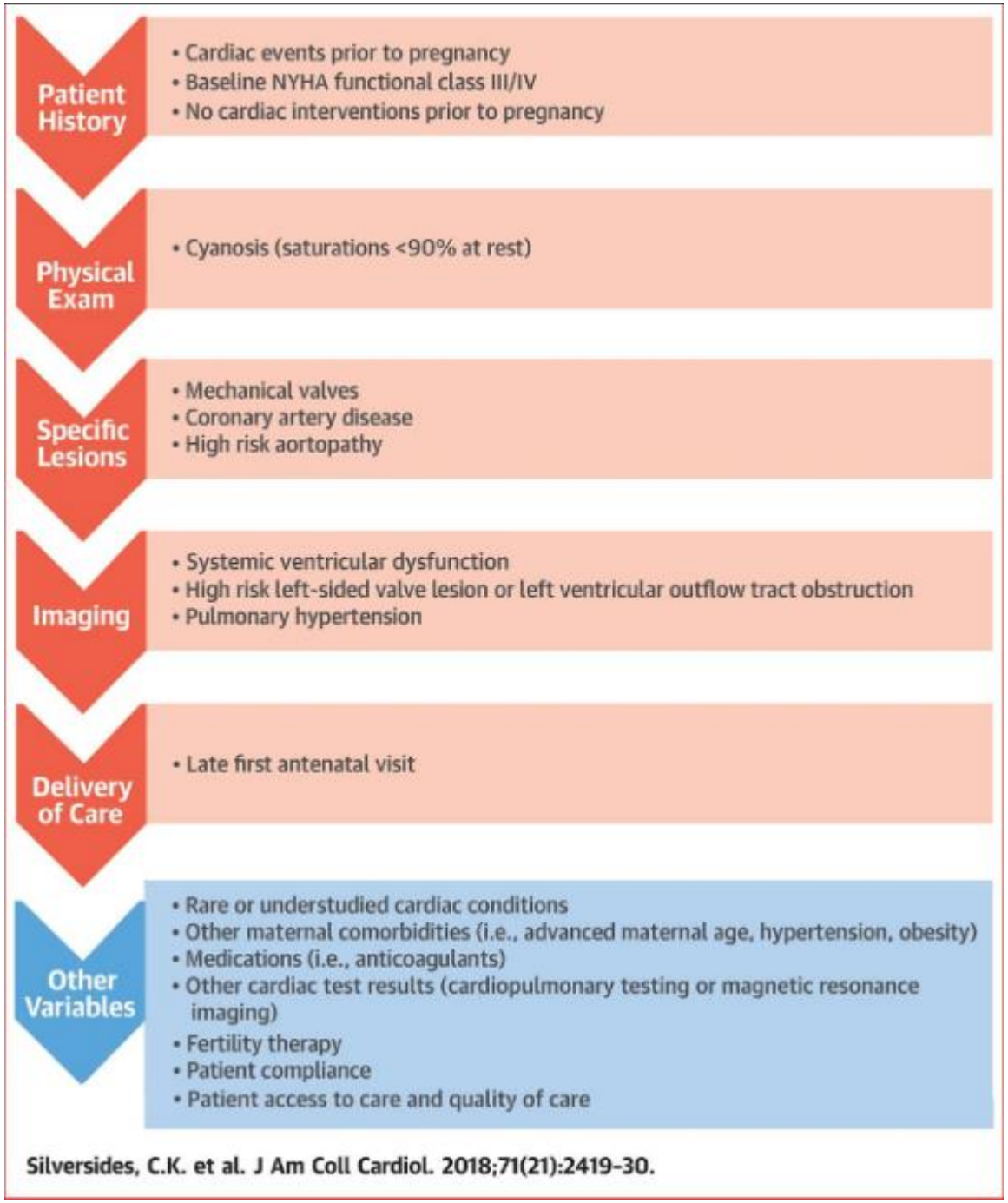
- Women at high or moderate risk of pre-eclampsia should be advised to take 100-150 mg of acetylsalicylic acid daily from week 12 to week 36-37 in addition to their hypertension treatment.
- Methyldopa, labetalol, and calcium antagonists are recommended for the treatment of hypertension in pregnancy.
- LMWH is the agent of choice for VTE prophylaxis and treatment.
- Thrombolytics to treat thrombo-embolism should only be used in patients with severe hypotension or shock.
- In the case of an emergency, drugs that are not recommended by the pharmaceutical industry during pregnancy and breastfeeding should not be withheld from the mother. The potential risk of a drug and the possible benefit of the therapy must be weighed against each other.



Silversides, C.K. et al. J Am Coll Cardiol. 2018;71(21):2419-30.

Conclusions

- Cardiovacsular diseases are the most frequent causes of maternal death in industrialised countries.
- The heterogeneity of heart diseases and inherent risks underline the need for an individual risk assessment and management.
- Counselling should start before pregnancy and may lead to prophylactic interventions.
- Interdisciplinary care should involve a team of gynecologists, cardiologists and others at each stage of pregnancy.
- High-risk women should be referred to specialised centres.