2023 HRS expert consensus statement on the management of arrhythmias during pregnancy

José A. Joglar, MD, FHRS (Chair),[1,*] Suraj Kapa, MD, FHRS (Vice-Chair),[2,*]
Elizabeth V. Saarel, MD, FHRS, CEPS-P (Vice-Chair),[3,*]
Anne M. Dubin, MD, FHRS, CEPS-P,[4,†] Bulent Gorenek, MD, FACC,[5,‡]
Afshan B. Hameed, MD, FACOG, FACC,[6,§] Sissy Lara de Melo, MD, PhD,[7,¶]
Miguel A. Leal, MD, FHRS,[8,*] Blandine Mondésert, MD,[9,*] Luis D. Pacheco, MD,[10,#]
Melissa R. Robinson, MD, FHRS, CCDS,[11,*] Andrea Sarkozy, MD, PhD, FEHRA,[12,**]
Candice K. Silversides, MD, FRCPC, FACC,[13,*] Danna Spears, MD,[14,*]
Sindhu K. Srinivas, MD, MSCE,[15,#] Janette F. Strasburger, MD,[16,†]
Usha B. Tedrow, MD, MS, FHRS,[17,*] Jennifer M. Wright, MD, MA, FHRS,[8,††]
Carolyn M. Zelop, MD, FAHA,[18,19,§] Dominica Zentner, MBBS (Hons), FRACP, PhD[20,‡‡]

Document Reviewers: Elena Arbelo, MD, MSci, PhD; Carina Blomström-Lundqvist, MD, PhD; Barbara J. Deal, MD, MS; M. Cecilia Gonzalez Corcia, PhD, CEPS-P; Rajesh Kabra, MD, FHRS; Magdalena J. Lagamayo, MD; Torri Metz, MD; Sarah Obican, MD; Alejandro Olaya, MD; Nisha Parikh, MD, MPH; Andrea M. Russo, MD, FHRS; Kamala P. Tamirisa, MD, FHRS

From the [1]The University of Texas Southwestern Medical Center, Dallas, Texas, [2]Mayo Clinic, Rochester, Minnesota, [3]St. Luke's Health System, Boise, Idaho, and Cleveland Clinic Lerner College of Medicine at Case Western Reserve University, Cleveland, Ohio, [4]Stanford University, Palo Alto, California, [5]Eskişehir Osmangazi University, Eskişehir, Turkey, [6]University of California, Irvine, Irvine, California, [7]University of São Paulo, São Paulo, Brazil, [8]University of Wisconsin–Madison, Madison, Wisconsin, [9]Montréal Heart Institute, Montréal, Quebec, Canada, [10]The University of Texas Medical Branch at Galveston, Galveston, Texas, [11]University of Washington, Seattle, Washington, [12]University Hospital of Antwerp, University of Antwerp, Antwerp, Belgium, [13]University of Toronto, Toronto, Ontario, Canada, [14]University Health Network, Toronto, Ontario, Canada, [15]University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, [16]Children's Hospital of Wisconsin, Milwaukee, Wisconsin, [17]Brigham and Women's Hospital, Boston, Massachusetts, [18]The Valley Health System, Ridgewood, New Jersey, [19]New York University Grossman School of Medicine, New York, New York, and [20]The University of Melbourne, Melbourne, Victoria, Australia.

**Representative of the Heart Rhythm Society (HRS)*
†Representative of the Pediatric and Congenital Electrophysiology Society (PACES)
‡Representative of the American College of Cardiology (ACC)
§Representative of the American College of Obstetricians and Gynecologists (ACOG)
¶Representative of the Latin American Heart Rhythm Society (LAHRS)
#Representative of the Society for Maternal-Fetal Medicine (SMFM)
***Representative of the European Heart Rhythm Association (EHRA)*
††Representative of the American Heart Association (AHA)
‡‡Representative of the Asia Pacific Heart Rhythm Society (APHRS)

 https://doi.org/10.1016/j.hrthm.2023.05.017

Abstract

This international multidisciplinary expert consensus statement is intended to provide comprehensive guidance that can be referenced at the point of care to cardiac electrophysiologists, cardiologists, and other health care professionals, on the management of cardiac arrhythmias in pregnant patients and in fetuses. This document covers general concepts related to arrhythmias, including both brady- and tachyarrhythmias, in both the patient and the fetus during pregnancy. Recommendations are provided for optimal approaches to diagnosis and evaluation of arrhythmias; selection of invasive and noninvasive options for treatment of arrhythmias; and disease- and patient-specific considerations when risk stratifying, diagnosing, and treating arrhythmias in pregnant patients and fetuses. Gaps in knowledge and new directions for future research are also identified.

TABLE OF CONTENTS

KEYWORDS Antiarrhythmic; Atrial fibrillation; Bradyarrhythmia; Fetal arrhythmia; Inherited arrhythmia syndrome; Maternal arrhythmia; Pregnancy; Supraventricular tachycardia; Tachyarrhythmia; Ventricular tachycardia

ABBREVIATIONS **3D** = 3-dimensional; **ACLS** = advanced cardiac life support; **ACM** = arrhythmogenic cardiomyopathy; **AF** = atrial fibrillation; **AFL** = atrial flutter; **AT** = atrial tachycardia; **AV** = atrioventricular; **BLS** = basic life support; **bpm** = beats per minute; **BrS** = Brugada syndrome; **CHD** = congenital heart disease; **COR** = class of recommendation; **CPR** = cardiopulmonary resuscitation; **CPVT** = catecholaminergic polymorphic ventricular tachycardia; **ECG** = electrocardiogram; **EF** = ejection fraction; **fMCG** = fetal magnetocardiography; **HCM** = hypertrophic cardiomyopathy; **IART** = intra-atrial reentrant tachycardia; **IAS** = inherited arrhythmia syndrome; **ICD** = implantable cardioverter defibrillator; **ICM** = implantable cardiac monitor; **IST** = inappropriate sinus tachycardia; **IVIG** = intravenous immunoglobulin; **LOE** = level of evidence; **LQTS** = long QT syndrome; **LV** = left ventricular; **MRI** = magnetic resonance imaging; **PAC** = premature atrial contraction; **PSVT** = paroxysmal supraventricular tachycardia; **PVC** = premature ventricular contraction; **QTc** = corrected QT interval; **RVR** = rapid ventricular rate; **RWI** = relationships with industry and other entities; **SHD** = structural heart disease; **SQTS** = short QT syndrome; **SVT** = supraventricular tachycardia; **TdP** = torsades de pointes; **VF** = ventricular fibrillation; **VT** = ventricular tachycardia (Heart Rhythm 2023;20:e175–e259)

Developed in collaboration with and endorsed by the American College of Cardiology (ACC), the American College of Obstetricians and Gynecologists (ACOG), the American Heart Association (AHA), the Asia Pacific Heart Rhythm Society (APHRS), the European Heart Rhythm Association (EHRA), the Latin American Heart Rhythm Society (LAHRS), the Pediatric and Congenital Electrophysiology Society (PACES), and the Society for Maternal-Fetal Medicine (SMFM).
Correspondence: Heart Rhythm Society, 1325 G St NW, Suite 500, Washington, DC 20005. E-mail address: clinicaldocs@hrsonline.org.

Top 10 take-home messages

1. The most common arrhythmias seen in pregnant patients are generally benign, including sinus arrhythmia, supraventricular tachycardia, and premature beats, whereas life-threatening arrhythmias, such as hemodynamically significant supraventricular tachycardia or ventricular tachycardia, are significantly less common.
2. Atrial fibrillation is increasingly becoming the most common newly diagnosed sustained arrhythmia during pregnancy. Some therapeutic decisions for atrial fibrillation, such as a rate-control strategy versus rhythm control strategy, should be based on hemodynamic tolerance and underlying substrate as in nonpregnant patients, whereas others, such as anticoagulation therapy protocols, are specific to pregnancy.
3. Care of arrhythmias in the pregnant patient should involve a multidisciplinary engagement of cardiologists and/or electrophysiologists, pediatric electrophysiologists, maternal-fetal medicine subspecialists, anesthesiologists, and neonatologists to optimize outcomes for both the mother and the fetus/newborn.
4. When arrhythmias occur in pregnancy, both the mother and the fetus may be affected; thus, shared decision-making should include a discussion of the risks and benefits to both the mother and the fetus of antiarrhythmic drugs, specific procedures, and monitoring, as well as the risks of withholding such therapies.
5. Fetal arrhythmia management decisions should be considered in the context of any concomitant maternal arrhythmias or diagnoses (eg, fetal bradycardia in mothers with long QT syndrome). Treatment of fetal arrhythmias generally involves either maternal systemic administration of antiarrhythmic agents; rarely, such as in cases of fetal hydrops, direct fetal intramuscular injection or intraperitoneal injection of antiarrhythmic drugs may be necessary.
6. Management of hemodynamically significant maternal arrhythmias should emphasize the prompt use of the most effective therapy available (cardioversion, antiarrhythmic drug infusion, or catheter ablation) to terminate the ongoing arrhythmia and/or prevent recurrent arrhythmias, with appropriate fetal monitoring, and measures to minimize radiation exposure when catheter ablation is pursued.
7. Procedures such as catheter ablation and implantable devices, if indicated for arrhythmias with hemodynamic compromise or for sudden death prevention, can be performed at experienced centers with maximum possible mitigation of radiation exposure to the fetus, which is best achieved by overall reduction of total maternal radiation, since covering the maternal abdomen with a lead apron alone is generally of no benefit.
8. Due to the overall risk of aortocaval compression in pregnant patients, particularly in the third trimester, avoidance of prolonged supine positioning is warranted, especially during invasive procedures, with preference given to a left lateral tilt position to optimize hemodynamics.

9. Use of antiarrhythmic drugs during pregnancy and the postpartum period should largely be similar to use in nonpregnant patients with some exceptions for the sake of fetal safety: selecting drugs with the longest record of safe use during pregnancy and lactation; using the lowest effective dose; and periodically reevaluating the continued need for the same dose/type of antiarrhythmic, including during the postpartum period, in light of potential drug concentration in breast milk.
10. For parents with a suspected or known inherited arrhythmia syndrome, genetic screening and counseling should be provided, ideally by genetic counselors or providers who are trained or specialize in genetics, to assess potential fetal risks and for therapeutic optimization.

Section 1 Introduction

1.1. Preamble

The Heart Rhythm Society (HRS) has developed expert consensus documents that have guided clinical care in the management of cardiac arrhythmias since 1996. This HRS-led expert consensus statement was developed in collaboration with the American College of Cardiology (ACC), the American College of Obstetricians and Gynecologists (ACOG), the American Heart Association (AHA), the Asia Pacific Heart Rhythm Society (APHRS), the European Heart Rhythm Association (EHRA), the Latin American Heart Rhythm Society (LAHRS), the Pediatric and Congenital Electrophysiology Society (PACES), and the Society for Maternal-Fetal Medicine (SMFM). This clinical practice document is intended to provide comprehensive guidance to cardiac electrophysiologists, cardiologists, and other health care professionals on the management of cardiac arrhythmias in pregnant patients, including arrhythmias that occur in the mother and in the fetus.

1.2. Document scope and objectives

Recommendations for the management of patients with arrhythmias during pregnancy have been addressed historically within the bodies of broader-scope clinical practice documents, which are focused primarily on nonpregnant patient populations; therefore, the issues related to pregnancies are limited in scope and specific to the guidelines discussed. Providers are thus in the position of looking at several documents that may not all agree or even address unique management considerations for arrhythmias in pregnant patients. This expert consensus statement on the management of arrhythmias in the pregnant patient and fetus provides a broad and comprehensive resource for guidance in a format that can be referenced at the point of care. The primary goals of this document are as follows:

1. Introduce general concepts related to arrhythmias in both the patient and the fetus during pregnancy.
2. Discuss optimal approaches to diagnosis and evaluation of arrhythmias during pregnancy.
3. Review approaches to treatment of arrhythmias in the pregnant patient, including invasive and noninvasive treatments.
4. Identify disease- and patient-specific considerations when risk stratifying, diagnosing, and treating arrhythmias in pregnant patients.
5. Provide recommendations for management of fetal arrhythmias.

This expert consensus statement provides recommendations for care based on current evidence for best practices in the management of arrhythmias during pregnancy for patients of all ages. When evidence was lacking or contradictory, a consensus expert opinion was developed. Health benefits, side effects, and risks to both the pregnant patient and fetus were considered comprehensively in formulating the recommendations. This document is intended to set standards that can be applied worldwide, while recognizing that resources, availability of technology, disease prevalence, and health care delivery logistics vary in different parts of the world. This document is intended to improve the quality of patient care by providing practical guidance for the optimal management of pregnant patients and fetuses that reflects the current standard of care, with the understanding that some procedures are better performed, and some disease states are better managed, in settings where there is specific expertise. The recommendations are not a replacement for clinical judgment and are not intended to dictate management in every single scenario.

1.3. Editorial independence

This expert consensus statement was sponsored by the HRS and developed without commercial support; writing committee members volunteered their time to the writing and review efforts.

1.4. Organization of the writing committee

The writing committee consisted of experts from 6 countries in the fields of electrophysiology, cardiology, pediatric electrophysiology and cardiology, gynecology, maternal-fetal medicine, and obstetrics. Each writing committee member served as a representative of either the HRS or a collaborating society and was nominated according to each organization's processes. The HRS strives to ensure that the writing committee contains both requisite expertise and diverse representation from the broader medical community. This is achieved by selecting experts from a wide range of backgrounds representing different geographic regions, genders, races, ethnicities, intellectual perspectives, and scopes of clinical practice, and by inviting organizations and professional societies with related interests and expertise to participate as partners or collaborators.

HRS has rigorous policies and methods to ensure that documents are developed without bias or improper influence. The complete policy on relationships with industry and other entities (RWI) can be found in the *HRS Code of Ethics and Professionalism: Appendix C* and in the *HRS Clinical Document Development Methodology Manual and*

Policies. A majority of the writing committee was free of relevant RWI throughout the development of the document and sections with recommendations were written by the writing committee members who were free of relevant RWI. For full transparency, Appendix 1 is a comprehensive list of RWI (both relevant and not relevant to the document topic) disclosed by the writing committee members. Appendix 2 is a comprehensive list of RWI disclosed by the peer reviewers.

1.5. Evidence review and formulation of recommendations

This expert consensus statement was developed in accordance with the clinical practice document methodology processes detailed in the *HRS Clinical Document Development Methodology Manual and Policies: Executive Summary,*[1] and with the standards issued in 2011 by the Institute of Medicine (now National Academy of Medicine).[2]

Consensus statements are evidence based, and recommendations are derived from the synthesis of published data or from a consensus of expert opinion when data are not available. The writing committee reviewed evidence gathered by electronic literature searches (MEDLINE, PubMed, Embase, Cochrane Library). No specific year was chosen for the oldest literature. Some literature databases allow the use of certain symbols to search for different forms or spellings of a word. The asterisk (*) was used for truncation to search for all forms of a word, the plus symbol (+) was used to search for plural and singular forms of a word, and the pound symbol (#) was used as a wildcard to search for variant spellings or hyphenation of a word. Search terms for this document included, but were not limited to the following: *Adams-stokes syndrome*, *adenosine*, *amiodarone*, *Andersen syndrome*, *anesthesia*, *anti#arrhythmic drugs*, *atenolol*, *atrial fibrillatio*n, *Afib*, *atrial flutter*, *arrhythmi**, *atrial premature complexes*, *atrioventric* block*, *AVB*, *beta#blocker+*, *bradycardia*, *Brugada*, *bundle#branch block*, *calcium channel blocker+*, *cardiac arrhythmia*, *cardiac sinus arrest*, *cardioversion+*, *catecholaminergic polymorphic ventricular tachycardia*, *CPVT*, *catheter ablation*, *defibrillat**, *defibrillator placement*, *delivery*, *digoxin*, *diltiazem*, *dofetilide*, *dronedarone*, *electric countershock*, *electrocardiograph**, *electroversion*, *evidence*, *fetal arrhythmia+*, *fetal magnetocardiograph**, *flecainide*, *fluoroscopy*, *heart block*, *inherited arrhythmia syndrome+*, *IAS*, *ibutilide*, *inherited arrhythmi**, *interatrial block*, *Jervell and Lange-Nielsen*, *JLNS*, *labetalol*, *labor*, *lidocaine*, *long QT*, *low fluoroscopy*, *Lown#Ganong#Levine*, *LGL*, *maternal anesthesia*, *metoprolol*, *mexiletine*, *no fluoroscopy obstetrical anesthesia*, *quinidine*, *parasystole*, *peripartum cardiomyopathy*, *post#partum*, *preconception counselling*, *pre#excitation*, *pregnan**, *premature cardiac complexes*, *procainamide*, *propafenone*, *radiation*, *risk stratification*, *Romano#Ward*, *short QT*, *sick sinus syndrome*, *sinus node dysfunction*, *sin#atrial block*, *SA block*, *sinus arrhythmia*, *sotalol*, *stillbirth*, *tachycardia*, *Torsades de Pointes*, *ventricular arrhythmia+*, *ventricular fibrillation*, *ventricular flutter*, *ventricular premature complexes*, *ventricular tachycardia*, *verapamil*, *wearable defibrillator*, *Wolff#Parkinson#White*. Literature searches focused whenever possible on randomized controlled trials, but systematic reviews, nonrandomized and registry studies, and cohort studies were included. Due to the limited randomized and/or blinded studies in the field of arrhythmia management in pregnant patients and fetuses, case series or registries and case reports that followed patients and documented outcomes were included in the evaluation of evidence to support recommendations in this document. Evidence tables are provided in Appendix 3 and summarize the evidence used by the writing committee to formulate recommendations. References are representative of the totality of data and are not meant to be all inclusive. Limitations of the evidence base are discussed in individual sections.

All recommendations were discussed by the writing committee, with consideration of the risks versus benefits of an intervention and the strength of the evidence. To assess consensus after discussions, the writing committee members participated in voting. A predefined threshold of 67% approval for each recommendation was required, with a quorum of two-thirds of the writing committee. An initial failure to reach consensus was resolved by subsequent discussions, revisions as needed, and revoting. The final mean consensus over all recommendations was 98.4%, with 123 of 163 recommendations receiving 100% consensus.

1.6. Class of recommendation and level of evidence

Recommendations in this expert consensus statement are designated with both a class of recommendation (COR) and a level of evidence (LOE) (Table 1).[3] The COR denotes the strength of the recommendation based on the assessment of the magnitude and certainty of the benefits in proportion to the risks. The LOE reflects the quality of the evidence that supports the recommendation based on type, quantity, and consistency of data from clinical trials and other sources.

For clarity and usefulness, each recommendation is linked to the supportive evidence through the specific references from the literature used to justify the LOE rating, which are also summarized in the evidence tables (Appendix 3). Each recommendation is accompanied by supportive text. Algorithms provide a summary of the recommendations, intended to assist clinicians at the point of care.

Table 1 ACC/AHA recommendation system: Applying class of recommendation and level of evidence to clinical strategies, interventions, treatments, and diagnostic testing in patient care (updated May 2019)*

CLASS (STRENGTH) OF RECOMMENDATION	
CLASS 1 (STRONG)	**Benefit >>> Risk**
Suggested phrases for writing recommendations: • Is recommended • Is indicated/useful/effective/beneficial • Should be performed/administered/other • Comparative-Effectiveness Phrases†: – Treatment/strategy A is recommended/indicated in preference to treatment B – Treatment A should be chosen over treatment B	
CLASS 2a (MODERATE)	**Benefit >> Risk**
Suggested phrases for writing recommendations: • Is reasonable • Can be useful/effective/beneficial • Comparative-Effectiveness Phrases†: – Treatment/strategy A is probably recommended/indicated in preference to treatment B – It is reasonable to choose treatment A over treatment B	
CLASS 2b (WEAK)	**Benefit ≥ Risk**
Suggested phrases for writing recommendations: • May/might be reasonable • May/might be considered • Usefulness/effectiveness is unknown/unclear/uncertain or not well-established	
CLASS 3: No Benefit (MODERATE) (Generally, LOE A or B use only)	**Benefit = Risk**
Suggested phrases for writing recommendations: • Is not recommended • Is not indicated/useful/effective/beneficial • Should not be performed/administered/other	
CLASS 3: Harm (STRONG)	**Risk > Benefit**
Suggested phrases for writing recommendations: • Potentialy harmful • Causes harm • Associated with excess morbidity/mortality • Should not be performed/administered/other	

LEVEL (QUALITY) OF EVIDENCE‡	
LEVEL A	
• High-quality evidence‡ from more than 1 RCT • Meta-analyses of high-quality RCTs • One or more RCTs corroborated by high-quality registry studies	
LEVEL B-R	**(Randomized)**
• Moderate-quality evidence‡ from 1 or more RCTs • Meta-analyses of moderate-quality RCTs	
LEVEL B-NR	**(Nonrandomized)**
• Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies • Meta-analyses of such studies	
LEVEL C-LD	**(Limited Data)**
• Randomized or nonrandomized observational or registry studies with limitations of design or execution • Meta-analyses of such studies • Physiological or mechanistic studies in human subjects	
LEVEL C-EO	**(Expert Opinion)**
• Consensus of expert opinion based on clinical experience	

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR 1 and 2a; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely-used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

Adapted with permission from the American College of Cardiology (ACC) and the American Heart Association (AHA).

1.7. Document review and approval

The HRS invites public and stakeholder involvement in document development, and draft recommendations were posted for public comment. This expert consensus statement was approved by the writing committee and underwent internal review and approval by the HRS Scientific and Clinical Documents Committee. The document underwent external peer review by reviewers appointed by HRS and each of the collaborating societies, and revisions were made by the writing committee chair and vice-chairs. A record of the writing committee's response to reviewer comments and rationale is maintained by HRS. The final document was sent to the collaborating societies for endorsement consideration.

1.8. Updating

The HRS Scientific and Clinical Documents Committee reviews each clinical practice document for currency at least every 5 years, or earlier in the event of newly published data. Literature is routinely monitored to evaluate the continued validity of recommendations.

1.9. Relevant clinical practice documents

Clinical practice documents relevant to the topic of arrhythmias during pregnancy were used to inform the development of this expert consensus statement. Table 2 lists applicable clinical practice documents (eg, guidelines and consensus statements) that the writing committee referenced during the development of this document.

Table 2 Relevant clinical practice documents

Title	Publication year
2021 European Heart Rhythm Association Practical Guide on the Use of Non-Vitamin K Antagonist Oral Anticoagulants in Patients With Atrial Fibrillation[4]	2021
2020 ESC Guidelines for the Diagnosis and Management of Atrial Fibrillation[5]	2021
2020 AHA/ACC Guideline for the Diagnosis and Treatment of Patients With Hypertrophic Cardiomyopathy[6]	2020
Cardiovascular Considerations in Caring for Pregnant Patients: A Scientific Statement from the American Heart Association[7]	2020
2019 ESC Guidelines for the Management of Patients With Supraventricular Tachycardia[8]	2020
2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation[9]	2019
2019 HRS Expert Consensus Statement on Evaluation, Risk Stratification, and Management of Arrhythmogenic Cardiomyopathy[10]	2019
2018 ACC/AHA/HRS Guideline on the Evaluation and Management of Patients With Bradycardia and Cardiac Conduction Delay[11]	2019
2018 ESC Guidelines for the Management of Cardiovascular Diseases During Pregnancy[12]	2018
2018 ESC Guidelines for the Diagnosis and Management of Syncope[13]	2018
Antiarrhythmic Drugs—Clinical Use and Clinical Decision Making: A Consensus Document from the European Heart Rhythm Association (EHRA) and European Society of Cardiology (ESC) Working Group on Cardiovascular Pharmacology[14]	2018
2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death[15]	2018
Management of Pregnancy in Patients With Complex Congenital Heart Disease: A Scientific Statement for Healthcare Professionals from the American Heart Association[16]	2017
European Heart Rhythm Association (EHRA) Consensus Document on the Management of Supraventricular Arrhythmias[17]	2017
2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients With Syncope[18]	2017
2015 ACC/AHA/HRS Guideline for the Management of Adult Patients With Supraventricular Tachycardia[19]	2016
2015 ACC/AHA/HRS Advanced Training Statement on Clinical Cardiac Electrophysiology (A Revision of the ACC/AHA 2006 Update of the Clinical Competence Statement on Invasive Electrophysiology Studies, Catheter Ablation, and Cardioversion)[20]	2016
Cardiac Arrest in Pregnancy: A Scientific Statement from the American Heart Association[21]	2015
Part 5: Adult Basic Life Support and Cardiopulmonary Resuscitation Quality: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care[22]	2015
Part 7: Adult Advanced Cardiovascular Life Support: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care[23]	2015
2015 ESC Guidelines for the Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death[24]	2015
Diagnosis and Treatment of Fetal Cardiac Disease: A Scientific Statement from the American Heart Association[25]	2014
Management of Patients With Atrial Fibrillation (Compilation of 2006 ACCF/AHA/ESC and 2011 ACCF/AHA/HRS Recommendations)[26]	2013
HRS/EHRA/APHRS Expert Consensus Statement on the Diagnosis and Management of Patients With Inherited Primary Arrhythmia Syndromes[27]	2013
HRS/EHRA Expert Consensus Statement on the State of Genetic Testing for the Channelopathies and Cardiomyopathies[28]	2011
ACCF/ASE/AHA/ASNC/HFSA/HRS/SCAI/SCCM/SCCT/SCMR 2011 Appropriate Use Criteria for Echocardiography[29]	2011

1.10. Definitions

The terms used in this expert consensus statement that are specific to pregnancy are defined in Table 3.

Table 3 Terms used in this consensus statement that are specific to pregnancy

Term	Definition
Cardio-obstetrics team	A group ideally composed of maternal-fetal medicine subspecialists, cardiologists and/or electrophysiologists (pediatric electrophysiologist when fetal arrhythmias are present), with experience managing pregnant patients. Neonatologists and anesthesiologists may also be involved close to the time of delivery. While the team may vary depending on the resources at a given facility, at a minimum it should include a high-risk obstetrician and a cardiologist with expertise in arrhythmias in pregnancy.[30]
Close to term	The term *close to term*, as used in this document, is purposely vague and not intended to represent a gestational age. The determination of a close-to-term fetus implies viability and considers a number of factors, such as severity and potential consequences of the arrhythmias, biological factors, and the site-specific availability of the medical expertise and technology to support a preterm infant. Close to term could fall within the gestational categories defined by the American College of Obstetricians and Gynecologists (ACOG): "late preterm" as 34 0/7 to 36 6/7 weeks of gestation, "early term" as 37 0/7 to 38 6/7 weeks of gestation, "full term" as 39 0/7 to 40 6/7 weeks of gestation, "late term" as 41 0/7 to 41 6/7 weeks of gestation, and "post term" as 42 0/7 weeks of gestation and beyond.[31,32]
Supine hypotensive syndrome	Supine hypotensive syndrome is a condition in which, while lying flat, a pregnant patient may become light-headed or syncopal due to compression of the inferior vena cava by the gravid uterus leading to reduction in venous return and resultant hypotension.

Section 2 General concepts for the management of arrhythmias during pregnancy

2.1. Epidemiology of arrhythmias

Apart from sinus tachycardia, the most common rhythm abnormalities in pregnancy are premature ventricular or atrial ectopic beats, seen in 50-60% of pregnant patients presenting with palpitations and generally resolving spontaneously after delivery.[33] Arrhythmias during pregnancy are more prevalent in the setting of structural heart disease (SHD); however, it is not uncommon for patients without an underlying cardiac defect to experience de novo rhythm disorders during pregnancy.[33-35] The increased propensity for patients to present with arrhythmias when pregnant is multifactorial and thought to be related to a combination of the hemodynamic, hormonal, and autonomic milieu changes that occur during pregnancy.[36]

Hospital admissions for arrhythmias are much less frequent than other general causes for admission during pregnancy.[37,38] The overall prevalence of arrhythmias among pregnancy-related hospitalizations is estimated at 68-166 per 100,000 pregnancy-related admissions, depending on how these are defined.[38] In a study of 136,422 pregnancy-related hospitalizations between 1992 and 2000, 0.1% of the admissions were associated with arrhythmia. The most frequent arrhythmia diagnosis was sinus arrhythmia (60% of the diagnoses, 104 per 100,000 pregnancy-related hospitalizations) followed by atrial or ventricular extrasystole (19%) and paroxysmal supraventricular tachycardia (PSVT) (14%). Atrial fibrillation (AF) and atrial flutter (AFL) (1%), ventricular fibrillation (VF) (1%), and high-degree atrioventricular (AV) block (1%) were rarely diagnosed.[38] In the nationwide 2000-2012 US study by Vaidya et al[37] of more than 57 million admissions of pregnant patients, the frequency of sustained arrhythmias was estimated at 68 per 100,000 pregnancy-related hospitalizations. Of these, AF occurred in 27 per 100,000, supraventricular tachycardia (SVT) in 22 per 100,000, ventricular tachycardia (VT) in 16 per 100,000, and VF in 2 per 100,000 pregnancy-related hospitalizations. The frequency of arrhythmias (especially AF and VT) increased over the study period and was associated with a greater frequency of in-hospital death (5.9%) and maternal or fetal complications (36.5%) compared with pregnancy-related admissions without arrhythmias (0% and 21.8%, respectively; Figure 1).[37] This recent increase in AF and VT frequency in pregnancy might be explained by the increase in maternal age accompanied by increase in risk factors such as obesity, hypertension, and diabetes mellitus, which are also on the rise. Increased survival and more frequent pregnancy of patients with congenital heart disease (CHD) is another contributing factor. Fortunately, the rate of mortality from arrhythmias decreased from 5.7% to 3.7% during the same time period. Arrhythmias during pregnancy are more frequently seen in Black women compared with White women (116 vs 73 per 100,000; $P < 0.001$).[37]

Pregnancy may aggravate preexisting arrhythmias, especially in older women (199 per 100,000 at 41-50 years of age vs 55 per 100,000 at 18-30 years of age), and in women with CHD.[37-39] In the 1321 women enrolled in ROPAC (Registry Of Pregnancy And Cardiac disease), 17 (1.3%) had AF or AFL with a higher incidence (2.5%) noted in women with mitral valve disease.[39] This is not surprising given that AF/AFL is traditionally associated with mitral valve disease.[40] Life-threatening arrhythmias (VT, VF), and bradycardia/conduction system disorders are rare in pregnancy.[37]

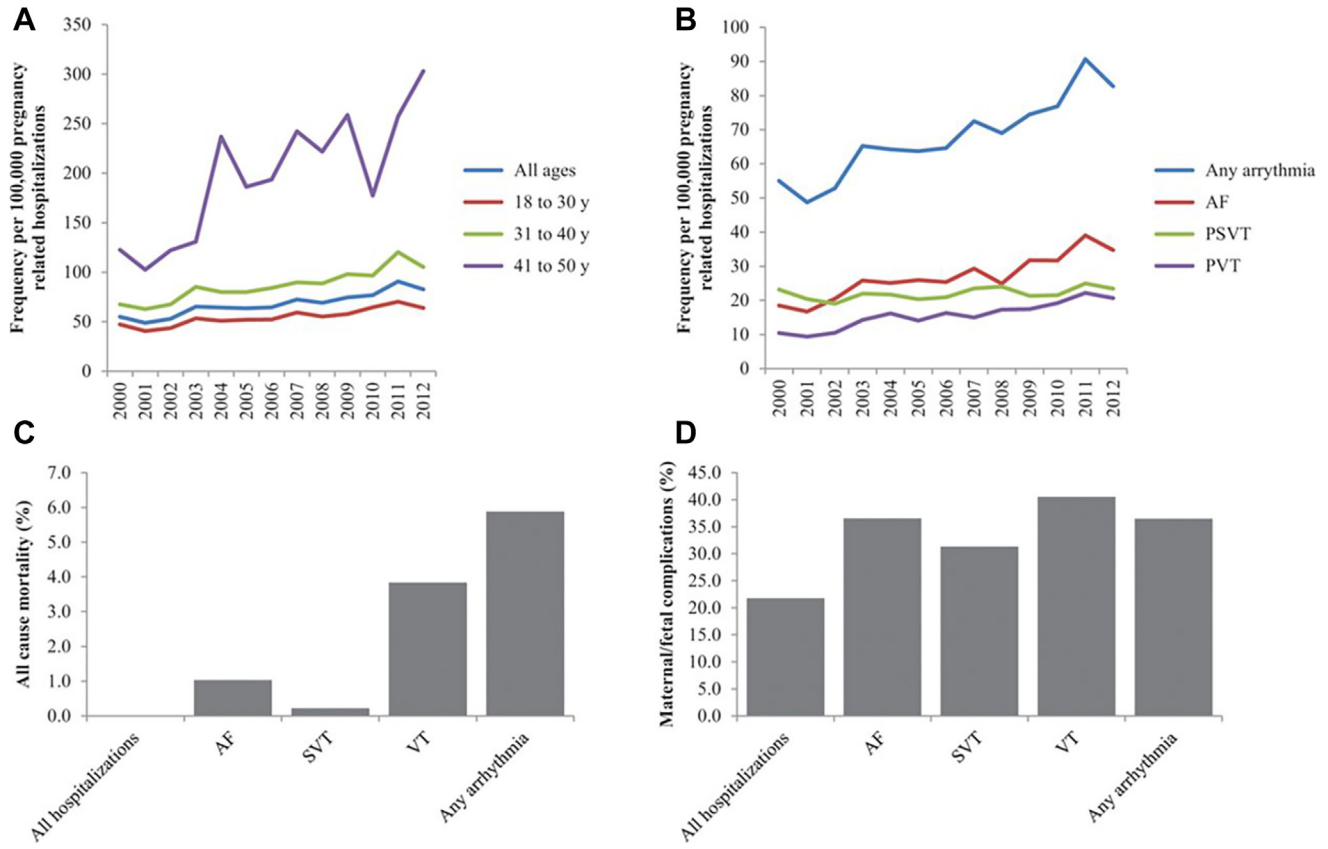

Figure 1 Frequency of arrhythmia in pregnancy and associated mortality and complications. **A**, Frequency of any arrhythmia per 100,000 pregnancy-related hospitalizations for the entire study period, stratified by age. **B**, Frequency of arrhythmias per 100,000 pregnancy-related hospitalizations by arrhythmia type for the entire study period. **C**, All-cause mortality in percentage for the entire study period. **D**, Perinatal complications (including preterm labor, ante- or postpartum hemorrhage, preeclampsia, eclampsia, gestational hypertension, transfusion, postpartum infection, and fluid and electrolyte imbalance) in percentages for the entire study period. Reprinted with permission from Vaidya et al.[37] AF = atrial fibrillation, PSVT = paroxysmal supraventricular tachycardia, PVT = paroxysmal ventricular tachycardia, SVT = supraventricular tachycardia, VT = ventricular tachycardia.

2.1.1. Etiology of palpitations

Palpitations, or unpleasant awareness of the beating heart, are among the most common cardiac symptoms during pregnancy and a frequent reason for referral to maternal-fetal medicine subspecialists or pregnancy-devoted cardiology clinics.[33,34,41] The exact incidence of palpitations during pregnancy is unknown, as patients frequently do not seek medical attention, but the spectrum of arrhythmias underlying the clinical symptom of palpitations ranges from benign conditions (eg, sinus tachycardia, atrial or ventricular extrasystole) to more serious arrhythmias (eg, PSVT, AF, life-threatening ventricular arrhythmias).

In a small study of 110 consecutive pregnancies with symptoms of palpitations, dizziness, or syncope (study group) and 52 pregnancies with asymptomatic functional precordial murmur (control group) undergoing Holter monitoring in an outpatient setting, 23% of patients in the control group reported palpitations during the 24-hour monitoring period.[33] In both the study and control groups there was a high incidence of premature beats but only 10% of the symptomatic episodes of palpitations during pregnancy were associated with an arrhythmia documented by 24-hour Holter monitoring in these women.[33] Increase in resting sinus rate during pregnancy is common, and one can expect a 10% or greater rise in resting heart rate due to autonomic, hemodynamic, and whole-body volume fluctuations. In the case of sinus tachycardia, inappropriate sinus tachycardia (IST) (defined as a resting heart rate >100, a mean ambulatory heart rate >90, and associated symptoms) has been reported to be associated with a higher frequency of induction at term, but with no impact on maternal or fetal outcomes.[42] Further, pregnancy is a common inciting event for IST, with about 8% of patients with IST identifying pregnancy as the inciting event. However, aside from symptoms, IST has not been associated with negative long-term outcomes.[43]

An arrhythmia that is documented during pregnancy can be the first onset of arrhythmia or the recurrence of a preexisting arrhythmia. In a study of 207 consecutive patients with PSVT referred for catheter ablation, only 3.9% of patients had first onset of PSVT in pregnancy. However, 22% of patients with PSVT prior to pregnancy had exacerbations of arrhythmia symptoms during pregnancy.[44] In a study of 73 patients with 87 pregnancies diagnosed with heart disease prior to pregnancy (69% with complex congenital or acquired heart disease), 44% developed recurrences of tachyarrhythmias during pregnancy. Recurrence rates during pregnancy in patients with a history of SVT, paroxysmal AF/AFL, and VT were 50%, 52%, and 27%, respectively. Adverse fetal events,

such as prematurity, occurred more frequently in pregnant patients with antepartum arrhythmias.[45] In several other studies, the presence of documented arrhythmia in pregnant patients with congenital or acquired heart disease was also an important risk factor for adverse maternal and fetal outcomes.[16,46]

2.1.2. Epidemiology and classification of syncope

Syncope is defined as a sudden, transient loss of consciousness due to global cerebral hypoperfusion. In a recent Canadian retrospective population-based cohort study of close to 500,000 live births between 2005 and 2014, the overall incidence of syncope during pregnancy was 1% (9.7/1000 pregnancies).[47] Patients with syncope were younger (age <25 years: 35% vs 21%; $P < 0.001$) and more likely primiparous (52% vs 42%; $P < 0.001$).

Syncope, a clinical symptom with a wide spectrum of underlying mechanisms and etiologies, is classified similarly in pregnant patients as in the general population, but supine hypotensive syndrome is unique to pregnancy (Table 4). Early studies reported that in late pregnancy 8% to 11% of women develop greater than 30%, or 30 mmHg, systolic blood pressure drop with or without symptoms when lying in supine position.[48,49] Symptoms may include dizziness, nausea, and—in rare cases—syncope. More recent magnetic resonance imaging (MRI) studies confirmed earlier angiographic findings and showed that the gravid uterus begins to compress the inferior vena cava in the supine position, beginning at the 20th week of pregnancy, with very severe obstruction at term.[50-52] Left tilt of ≥30 degrees or left lateral position of the pregnant patient increases the inferior vena cava volume and cardiac output significantly compared with supine position.[51,52]

The most frequent type of syncope occurring during pregnancy is reflex-mediated vasovagal syncope. Situational syncope occurs very rarely in pregnancy; in only 1 case report were 2 pregnant patients with micturition syncope reported.[53] Carotid sinus syndrome has not been described in pregnancy. It likely occurs very rarely in patients with a prepregnancy diagnosis of this condition. The prevalence of syncope in pregnancy due to orthostatic hypotension is unknown but may occur in patients with volume depletion due to severe bleeding or vomiting, or in patients taking medications for an underlying SHD. Blood pressure measurement in supine, sitting, and standing positions, with a detailed history taking, should point to the diagnosis in these patients. The exact prevalence of cardiac syncope in pregnancy is unknown (likely <1-2% of all syncope episodes), but it is very important in the differential diagnosis of syncope, as it is associated with higher risk of adverse fetal and maternal outcomes, such as premature birth and congenital abnormalities.[37,47] Sudden fast palpitations starting prior to syncope, preexisting diagnosis of tachyarrhythmias, underlying congenital or SHD or channelopathy, and family history of sudden death or arrhythmias should raise suspicion of underlying cardiac etiology. Detailed physical examination and 12-lead electrocardiogram (ECG) should further help in the differential diagnosis, similar to diagnosis of nonpregnant patients.[13,18]

Table 4 Main features and clinical characteristics for the classification of syncope

Classification of syncope	Main features	Clinical characteristics
I. **Neurally mediated reflex syncope**	**Mechanism is reflex-mediated bradycardia (cardioinhibitory type), vasodilatation (vasodepressor), or both (mixed type)**	**Typical prodrome: diaphoresis, nausea, vomiting, feeling warmth, pallor**
1. Vasovagal ○ Orthostatic ○ Emotional	○ Occurs in upright or sitting posture with specific triggers ○ Occurs in situational settings associated with high stress or intense emotions, such as fear or sadness	• Most common, history of preexisting episodes ○ Triggered by longtime standing ○ Triggered by fear, pain, sight of blood
2. Situational	• Occurs with specific triggers	• Micturition, coughing, defecation • Very rare in pregnancy, history of preexisting symptoms
3. Carotid sinus syndrome	• Occurs with specific triggers and can be reproduced with carotid sinus massage	• Head turning or pressure on neck at carotid sinus • Very rare in pregnancy, history of preexisting symptoms
II. Syncope due to orthostatic hypotension	**A drop in systolic BP >20 mmHg or diastolic BP >10 mmHg with assuming upright position**	**Exacerbated by thermal stress, or venous pooling during exercise or after meals**
1. Volume depletion		• May occur in pregnancy with hemorrhage or vomiting
2. Drug-induced	• Vasodilators or diuretics	• Rare in pregnancy

(*Continued*)

Table 4 Main features and clinical characteristics for the classification of syncope (*Continued*)

Classification of syncope	Main features	Clinical characteristics
3. Neurogenic	• Associated with systemic and/or neurological disease	• Preexisting autonomic nervous system failure • Very rare in pregnancy
III. Cardiac syncope		
1. Arrhythmic	• ECG documentation during symptoms is diagnostic • History of preexisting congenital or acquired heart disease or primary channelopathy	• History of preexisting symptoms/arrhythmia is frequent • No or little prodrome • Short duration (<10 seconds), quick recovery • Very rare in pregnancy
○ Tachyarrhythmia		○ Fast, paroxysmal palpitations prior to syncope
○ Bradyarrhythmia	○ History of preexisting congenital AV block	
2. Structural cardiovascular disease associated	• Obstruction to blood flow in the heart or great vessels • Preexisting HCM, aortic stenosis, tamponade, cardiac masses • Pulmonary embolism	• Associated symptoms and signs of underlying heart disease • Disease-specific dyspnea, heart failure, angina, cyanosis • Disease-specific ECG abnormalities
IV. Supine orthostatic hypotension and syncope	**Inferior cava compression by the gravid uterus in late pregnancy in supine position**	**Left lateral decubitus position obviates the symptoms**
V. Psychogenic pseudosyncope	**Apparent but not true loss of consciousness**	**Symptoms are reproduced at tilt table test with normal blood pressure, heart rate, and EEG activity**

AV = atrioventricular, BP = blood pressure, ECG = electrocardiogram, EEG = electroencephalogram, HCM = hypertrophic cardiomyopathy.

2.2. Physiological, hormonal, and autonomic changes related to arrhythmogenesis

Despite the fact that new-onset malignant cardiac arrhythmias during pregnancy are extremely rare in the absence of SHD, more benign rhythm disturbances—such as sinus tachycardia and premature atrial contractions (PACs), and premature ventricular contractions (PVCs)—are quite common, particularly in the latter half of pregnancy.[33]

Pregnancy-induced cardiovascular changes (including increased resting heart rate, increased blood volume resulting in cardiac chamber dilation with greater end diastolic volumes, and higher levels of placental-originated potentially arrhythmogenic hormones) may predispose pregnant patients to cardiac arrhythmias. Effective blood volume increases by 50% during gestation, and up to 100% in twin pregnancies, which may result in myocardial atrial and ventricular stretching that leads to activation of stretch-sensitive ion channels, with subsequent membrane depolarization, shortened refractoriness, slowed conduction, and spatial dispersion of refractoriness, resulting in potential arrhythmogenesis.[54,55] Similarly, pregnancy-induced heart chamber enlargement increases the length of reentrant pathways, facilitating development of reentrant arrhythmias.[55]

Pregnancy-induced increases in estradiol, progesterone, and free cortisol may also predispose pregnant patients to cardiac arrhythmias. Both animal and human studies have described the arrhythmogenic potential of estrogen and progesterone by increasing the number and responsiveness of adrenergic receptors within the myocardium.[56,57]

Lastly, at the autonomic level, as pregnancy progresses there is a shift from a vagal to a higher sympathetic milieu, resulting in an increase in basal heart rate of 10 to 20 beats per minute (bpm).[58] An increase in resting heart rate has been associated with a higher risk of new-onset arrhythmias among nonpregnant individuals.[55] This increased sympathetic tone may predispose pregnant patients to new-onset arrhythmias or worsening burden of previous rhythm disturbances in those with a preexisting arrhythmic substrate.

2.3. General considerations for antiarrhythmic drugs in pregnancy

The overall approach to the treatment of arrhythmias in a pregnant patient is largely similar to the approach in a nonpregnant patient, but with modifications based on fetal safety. Importantly, the care of a pregnant patient with hemodynamically significant arrhythmias should not be compromised for fear of providing needed treatment in pregnancy, or potentially exposing the fetus to risk, since restoration of normal hemodynamics is the priority. Unfortunately, knowledge about specific medications/strategies in pregnancy or during breastfeeding is limited by a lack of robust scientific data. When pharmacological therapy is deemed necessary, a risk-versus-benefit discussion of maternal health and pregnancy outcomes should occur that considers treatment guide-

lines for the arrhythmic condition, the mechanisms of action of the drug (or class of drug), the record of safe use of the drug during pregnancy, and the potential overall risk of the treatment. The use of antiarrhythmic drugs in pregnancy requires attention to potential changes in pharmacokinetics due to the changes in maternal physiology, such as metabolism and an increase in intravascular volume.[59,60] For example, intravascular volume changes peak in the third trimester of pregnancy and pregnant patients often require a medication increase to achieve the same intended clinical effect. Therefore, it is important to monitor drug levels or, alternatively, to monitor the physiological effect of drugs (eg, ECG monitoring for QT prolongation).[59]

Maternal therapy with beta-blockers during pregnancy has been associated with intrauterine fetal growth restriction. Most of the studies on maternal beta-blocker therapy are based on pregnant patients with hypertensive disorders of pregnancy, where fetal growth could be affected by the underlying condition, in this case hypertension, and not necessarily the drug itself.[61] However, a study of beta-blockers prescribed for maternal cardiac conditions, with a separate analysis of pregnant patients with isolated tachyarrhythmias as the indication, demonstrated a significant effect of beta-blockers on fetal growth after adjusting for other potential confounders.[62] Although concern regarding fetal growth restriction has been highlighted for atenolol and labetalol particularly, it is important to recognize that the maternal indication for medications differed among the different beta-blockers, and the overrepresentation of maternal hypertensive disorders in these subgroups may have affected the results significantly.[63] In a review of cardiovascular medications in pregnancy, atenolol had a former United States Food and Drug Administration (FDA) risk category D rating for its use during pregnancy.[64] In a more recent study, Grewal et al[65] reported the birth weight reduction associated with beta-blockers to be less than 200 grams, and therefore not of great clinical consequence in most instances. Thus, in the setting of potentially life-threatening scenarios (eg, some inherited arrhythmia syndromes [IAS]) a maternal indication for prescription of a beta-blocker takes priority over potential fetal growth-restriction concerns, and beta-blocker therapy should be continued during pregnancy and the postpartum period (Figure 2). Dosages and risks for common antiarrhythmic drugs are outlined in Table 5. Additional resources for drug safety during pregnancy include MotherToBaby (https://mothertobaby.org), Reprotox (https://reprotox.org/member), and Teris (https://deohs.washington.edu/teris/).

During lactation, special consideration should be given to medications that may adversely affect the newborn. While some medications are safe in pregnancy, their metabolism and concentration in breast milk can be of concern during lactation. One example of this is the beta-blocker nadolol, which has a high concentration in breast milk.[66] The excretion of beta-blockers into breast milk is largely determined by the degree of protein binding; medications with low binding are more heavily excreted into breast milk.[67] For example, based on protein binding and renal excretion, nadolol presents a high risk for accumulation in infants. If clinically acceptable for the maternal cardiac indication, propranolol or metoprolol might be preferred over nadolol in breastfeeding. Yet the discussion of medications during breastfeeding should include consideration of the underlying conditions of the pregnant patient, the optimal treatment for their arrhythmia, and whether there is a reasonable alternative that has similar efficacy but is safer for breastfeeding (Figure 2). If there are no medication alternatives that are efficacious for the patient and safe with lactation, lactation may need to be avoided or monitored closely for potential side effects (eg, excess bradycardia in the case of nadolol). This decision should be based on a shared decision-making discussion with the patient and family that considers the negative impact of deferring the recommended pharmacological therapy on maternal health in the postpartum period balanced against the importance of breastfeeding to the postpartum patient and baby. Risks of antiarrhythmic drugs during lactation are outlined in Table 5. More information on drug safety during lactation can be found in the Drugs and Lactation Database (LactMed) (https://www.ncbi.nlm.nih.gov/books/NBK501922).

Prior to 2015, the FDA used a 5-tier set of alphabet categories (A, B, C, D, and X), introduced in 1979, to designate the safety of a drug for use during pregnancy (Figure 3).[64] The system was simple to understand for category A drugs, which were generally safe to use, and category X drugs, which were contraindicated. However, because the category system did not accurately or consistently communicate differences in degrees of fetal risk, its implementation led to misinterpretation and avoidance of drug categories B, C, and D, which generally had limited or ambiguous data Thus, on June 30, 2015, the FDA introduced the new Pregnancy and Lactation Labeling Rule to replace the prior risk categories and to help physicians better communicate the potential drug risks to patients during pregnancy and lactation (Figure 3).[70,71] Under the Pregnancy and Lactation Labeling Rule, package

	Propranolol	Metoprolol	Nadolol	Atenolol	Mexiletine	Quinidine	Sotalol
Use during pregnancy	Safe	Safe	Safe	Risk	Caution	Safe	Safe
Use when breastfeeding	Safe	Safe	Caution	Risk	Caution	Safe	Safe

Figure 2 Antiarrhythmic drug safety for commonly used drugs in pregnancy.[68,69]

inserts are now to contain individualized narrative summaries for each medication that include the "risks of using a drug during pregnancy and lactation, a discussion of the data supporting that summary, and relevant information to help health care providers make prescribing decisions and counsel women about the use of drugs during pregnancy and lactation"[71] (p. 72064) Despite this change, a recent study reported that human data on pregnancy and lactation are available in less than 20% of new product labeling.[72]

Prior Labeling

Pregnancy risk categories				
A	**B**	**C**	**D**	**X**
Adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in the first trimester of pregnancy	Animal reproduction studies have failed to demonstrate a risk to the fetus, and there are no adequate and well-controlled studies in pregnant women, **or** animal reproduction studies have shown adverse effects, but well-controlled studies in pregnant women have shown no adverse effects to the fetus	Animal reproduction studies have shown an adverse effect on the fetus, or there are no animal reproduction studies and no well-controlled studies in humans	Positive evidence of fetal risk, but benefits may outweigh risks	Positive evidence of fetal risk, and risks clearly outweigh any possible benefit

Sections		
Pregnancy	**Labor and delivery**	**Nursing mothers**

Pregnancy Lactation Labeling Rule

Sections		
Pregnancy	**Lactation**	**Female and males of reproductive potential***
Pregnancy exposure registry If there is a pregnancy registry that is scientifically acceptable, contact information needed to enroll or to obtain information about the registry. **Risk summary** Summary of the risks of using a drug during pregnancy including risk to the fetus and a general statement about background risk, or a statement if the drug is not absorbed systemically. **Clinical considerations** Relevant information, if it is available, to help health care providers make prescribing decisions and counsel women about the use of the drug during pregnancy under the headings: • Disease-associated maternal and/or embryo/fetal risk • Dose adjustments during pregnancy and the postpartum period • Maternal adverse reactions • Fetal/neonatal adverse reactions • Labor or delivery **Data** Discussion of human and animal data relevant to the risk summary.	**Risk summary** If data demonstrate that the drug is not absorbed systemically: • A specified statement regarding this fact. If data demonstrate that the drug is absorbed systemically by the mother: • Relevant information on the presence of the drug in human milk, effects of the drug on the breastfed child, and effects of the drug on milk production. A risk and benefit statement must appear at the end of the summary of risks unless breastfeeding is contraindicated during drug therapy. **Clinical considerations** Relevant information concerning ways to minimize drug exposure in the breast-fed child in certain situations and concerning available interventions for monitoring or mitigating the adverse reactions. **Data** Discussion of human and animal data relevant to the risk summary.	**Pregnancy testing** **Contraception** **Infertility** Relevant information when pregnancy testing or contraception is required or recommended before, during, or after drug therapy or when there are human or animal data that suggest drug-associated fertility effects, under the subheadings above.

Figure 3 Comparison of prior (1979) FDA pregnancy risk categories to the (2015) Pregnancy and Lactation Labeling Rule, which eliminated the pregnancy risk categories and provides individualized summaries of risk for each medication.[70,71] *Only included when there are recommendations or requirements for pregnancy testing and/or contraception before, during, or after drug therapy, and/or there are human and/or animal data suggesting drug-associated effects on fertility and/or preimplantation-loss effects.

Table 5 Antiarrhythmic drugs for use in pregnancy*[25,64,73-96]

Drug	Therapeutic maternal dose range†	Therapeutic maternal serum level	Toxicity/adverse events	
			Maternal	Fetal/neonatal
Digoxin[80,82,97-100] (mat/fetal PO, IV, direct fetal IM, IC)	**LD:** 1.5-2.0 mg/24 h PO/IV, divided Q 8 h **MD:** 0.125-0.5 mg/day PO, divided BID **DFT:** (fetal IM dose 88 μg/kg, then 60-88 μg/kg fetal IM Q 12 h × 2)	0.7-2.0 ng/mL F/M ratio @ 50-100%; in hydrops 20%	N/V+++, anorexia++, sinus bradycardia+ or Mobitz I AV block+, proarrhythmia +, avoid in WPW	Fetal IM: sciatic nerve injury (~1:40 risk); fetal IC: cardiac arrest, consider IC or ICard epinephrine if this occurs Infant: Usually well tolerated, often used in combination, vomiting++, sinus bradycardia++, AV block, proarrhythmia
Class IA: Na^+ channel blockers				
Procainamide[83,96] (mat IV, +/− PO)	**LD:** 15 mg/kg IV over 30 min **MD:** 1-4 mg/min infusion	4-8 μg/mL	N/V+, TdP, ↑QTc, IV, uterine irritability, preterm labor	Neonatal TdP+, ↑QTc
Quinidine gluconate[101-103] (mat/fetal IV, PO)	**LD:** 200-400 mg PO Q 2-3 h until therapeutic effect (max 3 g/day) **MD:** XR 324-648 mg Q 8-12 h Parenteral: 10 mg/kg over 1-2 h, then 0.02 mg/kg/min × 72 h	2-6 mg/L F/M ratio 30-100%	N/V+++, CNS+, ↑QTc+, proarrhythmia, TdP	Neonatal TdP, concentrates in breast milk
Class IB: Na^+ channel blockers				
Lidocaine[104-106] (mat/fetal IV)	**LD:** 1-1.5 mg/kg LD IV, 300 mg max **MD:** infusion of 1-4 mg/min	1.5-5 μg/mL F/M ratio 1:1	N/V++, CNS+, proarrhythmia (consider all sources of lidocaine, including regional anesthesia) can halt labor	CNS++, bradycardia during labor (consider all sources of lidocaine, including regional anesthesia)
Mexiletine[107] (mat/fetal PO)	**LD:** 6-8 mg mg/kg/day Q 8-12 h (up to 400 mg Q 8 h or 450 mg Q 12 h) **MD:** 200-300 mg TID	0.5-2 μg/mL F/M ratio 1:1	NV++, CNS++, proarrhythmia	CNS++, concentrates in breast milk
Class IC: Na^+ channel blockers				
Flecainide[90,98,108-111] (mat/fetal PO)	**MD:** 200-400 mg/day divided Q 8-12 h PO Avoid in SHD	0.2-1.0 μg/mL F/M ratio 50-86%	Visual/CNS++, mild P/QRS widening + and 1° AV block+, ↑QTc, AFL	Fetal/neonatal QRS widening with longer exposure (drug concentrates in amniotic fluid); ↑QTc+, proarrhythmia+; well tolerated in infants, commonly combined with other drugs
Propafenone[112-115] (mat/fetal PO)	**MD:** 150 mg Q 8 h, increase slowly (max 900 mg/day), extended release 225-425 Q 12 h PO Avoid in SHD	500-600 ng/mL (range 65-1000) F/M ratio NA	CNS++, ↑QTc, GI+, QRS widening, AFL, bradycardia	CNS+, little data

(*Continued*)

Table 5 Antiarrhythmic drugs for use in pregnancy*[25,64,73-96] (*Continued*)

Drug	Therapeutic maternal dose range†	Therapeutic maternal serum level	Toxicity/adverse events	
			Maternal	Fetal/neonatal
Class II: Beta-blockers				
Propranolol[88,116-121] (mat/fetal PO, IV)	**MD:** 60-320 mg/day divided Q 6-12 h Parenteral (caution): 1-3 mg IV at <1 mg/min, can repeat once; reserve for life-threatening arrhythmia	25-140 ng/mL F/M ratio 0.4	Fatigue++, bradycardia++, hypotension++, AV block, ↑uterine tone	
Metoprolol[116,122,123] (mat/fetal PO/IV)	**MD:** 50-450 mg/day PO, divided BID if SR or Q 6 h if standard Parenteral (caution): 5 mg Q 2 min × 3 then change to PO; for HTN, labetalol preferred	5-10 ng/mL	Similar to propranolol	
Nadolol[116,122] (mat PO)	**MD:** 40-80 mg/day PO; up to 240 mg has been used	Not used clinically	Same as other beta-blockers; noncompliant patients may maintain levels due to long T1/2	
Class III: K^+ channel blockers and multimechanism				
Sotalol[75,78,80,81,87,98-100,108,115,124,125] (mat/fetal PO, mat PO/IV)	**MD:** 160-320 mg/day divided BID or Q 8 h Parenteral for life-threatening maternal arrhythmia: 75-150 mg IV Q day or BID (if QTc <450 ms)	200-1000 ng/mL, fetal can be > maternal, F/M ratio 100-107%	N/V/fatigue/CNS++, sinus bradycardia+, ↑QTc (hold or reduce dose if QTc >500 ms), proarrhythmia	CNS, +/-proarrhythmia, bradycardia+, (concentrates in amniotic fluid), rare ↑QTc; well tolerated in infants
Amiodarone[106,108,126-130] (mat/fetal PO, mat IV, DFT)	**LD:** 1800-2400 mg/day PO divided Q 6 h × 48 h; lower LD (1200 mg) if concurrent drug therapy; no fetal advantage to maternal IV dosing Maternal parenteral LD: 1000 mg over 24 h as 150 mg/10 min, then 360 mg/6 h, then 540 mg/18 h IV **MD:** 800 mg × 1 wk, then 200–600 mg/day; Maternal parenteral MD: 0.5 mg/min IV up to 3 wk **Cardiac arrest:** 5 mg/kg (max 300 mg) rapid IV/IO/ET, repeat 1-2× **DFT (hydrops only):** IC 2.5-5 mg/kg nonhydropic fetal weight up to 40 mg, diluted with glucose and given over 5-10 min; intraperitoneal 50-75 mg in D5W, repeat as needed, can remove excess ascitic fluid prior to amiodarone administration	0.7-2.8 μg/mL F/M ratio 10-30%, but efficacy over time is seen due to fatty-tissue accumulation	NV++, ↑thyroid++, sinus bradycardia+++, ↓appetite, 1° AV block, P/QRS widening, ↑QTc, proarrhythmia, photosensitivity rash, TdP, ↑other drug concentrations (digoxin, flecainide), liver and lung toxicity with chronic use Parenteral: hypotension if doses >2100 mg/24 h	↑Thyroid++, fetal TdP if given for LQTS, goiter, neurodevelopmental concerns Intracordal: fetal death++ Intraperitoneal: possible GI adhesions (1 report only) Amiodarone, despite its side effects, can allow fetal survival in severe cases, especially prior to preterm delivery of a severely hydropic fetus <35 wk GA; often used in combination with other drugs, and may take several weeks to slow, and then terminate tachycardia Absence of progression of hydrops is usually a sign of early improvement

(*Continued*)

Table 5 Antiarrhythmic drugs for use in pregnancy*[25,64,73-96] (*Continued*)

Drug	Therapeutic maternal dose range†	Therapeutic maternal serum level	Toxicity/adverse events	
			Maternal	Fetal/neonatal
Class III: K^+ channel blockers and multimechanism *(Continued)*				
Ibutilide[82,131,132] (mat only, IV only)	**LD:** for acute termination of drug-refractory atrial tachyarrhythmia: <60 kg = 0.01 mg/kg IV over 10 min, may repeat after 10 min >60 kg = 1 mg IV over 10 min, may repeat after 10 min	NA	QT prolongation, TdP, hold other QT prolonging drugs before and after; telemetry for at least 4 h post-infusion	Embryotoxic, teratogenic, avoid in first trimester
Dronedarone	Contraindicated in pregnancy			Fetal harm from visceral and skeletal malformations in animal studies
Class IV: Calcium channel blockers				
Verapamil[133] (mat only IV, PO)	**LD:** 5-10 mg IV, can repeat after 30 min **MD:** 120-480 mg/day PO	125-400 μg/mL	(Substitute with adenosine or beta-blocker if possible) mat hypotension, uterine muscle relaxant	Embryotoxic, fetal bradycardia, fetal hypoxia Infant: hypotension, hypocontractility, fetal demise, jaundice, seizures, hetatologic abnormalities; Concentrates in breast milk
Diltiazem[83] (mat only IV, PO)	**LD:** 0.25 mg/kg IV over 2 min, repeat 0.35 mg/kg, then 5-15 mg/h IV infusion (start immediately after bolus) **MD:** XR 180-360 mg PO Q day	50-200 ng/mL	CNS++, potent vasodilator++, hypotension, bradycardia, uterine muscle relaxant	Embryotoxic, fetal demise, hypocontractility, M/F serum:breast milk = 1:1
Other arrhythmia drugs				
Adenosine[25] (mat IV)	**LD:** 6-12 mg rapid IV, up to 24 mg has been used	NA	Flushing, transient chest pain and bradycardia	Safe for fetus when mother is treated IV; not useful for treatment of fetal SVT Intracordal: nonsustaining cardioversion, fetal demise
Atropine (mat IV)	**LD:** 0.02 mg/kg IV, repeat Q 3-5 min for cardiac arrest (max 3 mg), lower doses for acute 2:1 AV block	Not used	Rebound sinus tachycardia; improvements in AV conduction may be transient	F/M ratio 0.13
Magnesium sulfate[134] (mat/fetal IV, then PO)	**LD:** 2-6 g IV over 20 min **MD:** 1-2 g/h; treatment for >48 h is generally avoided though may consider redosing if VT recurs; PO 200-600 mg/day	<6 mEq/L; monitor elbow and patellar reflexes	GI++, fatigue++, CNS++ symptoms; STOP for loss of patellar reflex and/or levels >6 mEq/L; levels >5 mEq/L associated with maternal ECG changes and proarrhythmia	Hypotonia+, lower assigned Apgar scores

*The PDR (Prescriber's Digital Reference) website (https://www.pdr.net/) is an additional resource; the information provided may vary from the PDR based on other evidence for antiarrhythmic drug use during pregnancy and lactation.

†Dosages may vary from those listed in the Food and Drug Administration–approved labeling (available at https://dailymed.nlm.nih.gov/dailymed/) and are not meant to replace clinical judgment. Drug doses provided here can be used for either maternal or fetal treatment. Maternal use, fetal use, or both are noted in the first column along with the routes available. Treatment during pregnancy requires a strong knowledge of pregnancy pharmacokinetics and is best done by the cardio-obstetrics team (Section 3.2). The lowest effective drug dose should be used, but higher drug doses may be required during the latter part of pregnancy to maintain therapeutic serum concentrations. In general, all of these drugs are started during a hospital stay. When intravenous drugs are used, telemetry, electrocardiogram (ECG), and blood pressure monitoring are important. For chronic outpatient administration, consider long-acting preparations if available. Transplacental drug treatment does not necessarily require continuation of the drug until delivery and does not mandate the need for neonatal drug therapy.

+++ = very common, ++ = common, + = occasional, AFL = atrial flutter, AV = atrioventricular, CNS = central nervous system, DFT = direct fetal therapy, F = fetal, GA = gestational age, GI = gastrointestinal, HTN = hypertension, IC = intracordal, IM = intramuscular, IV = intravenous, LD = loading dose, LQTS = long QT syndrome, M or Mat = maternal, MD = maintenance dose, NA = not applicable, N/V = nausea and vomiting, PO = by mouth, proarrhythmia = worsening of an arrhythmia as the result of treatment, QTc = corrected QT interval, SHD = structural heart disease, SVT = supraventricular tachycardia, SR = sustained-release, TdP = torsades de pointes, WPW = Wolff-Parkinson-White syndrome, VT = ventricular tachycardia.

2.4. General considerations for management of fetal arrhythmias

General principles for pharmacological therapy of fetal arrhythmias depend on factors such as underlying etiology, presence of cardiac failure (fetal hydrops), and gestational age (which may prompt delivery of a close-to-term fetus in lieu of in utero treatment). Maternal thyroid disease is common in pregnancy, and the mother should be treated if this is identified as the likely precipitant of fetal arrhythmias. The most common cause of referral for a fetal arrhythmia usually involves the presence of PACs or ventricular contractions. These are usually benign and, in the absence of SHD, do not require additional antenatal surveillance or changes in delivery planning.

For a fetus with a channelopathy, avoidance of exacerbating maternal electrolyte abnormalities and medications is crucial. Additionally, it is important to educate pregnant patients and their partners with genetic conditions such as long QT syndrome (LQTS), in which fetal bradycardia most likely represents an in utero manifestation of the underlying diagnosis rather than an adverse effect of maternal medication. In that setting, the bradycardia should not lead to cessation of maternal beta-blocker therapy.[15]

Sustained fetal tachycardias are usually treated by transplacental (maternal) administration of antiarrhythmic drugs, unless delivery is determined to be the most appropriate approach. As such, pharmacological considerations are usually based on maternal dosing. Direct fetal administration has been described in hydropic fetuses where absorption is likely to be inadequate.[25] The placenta is both a physical barrier as well as a metabolic interface between the maternal and fetal circulations. Though not well understood, it is quite likely that the amount of medication delivered to the fetus varies during the course of gestation.[135] Additionally, it is important to acknowledge that there is at the present no randomized trial of medical therapy for fetal arrhythmias,[136] and that treatment algorithms rely on observational studies, local experience, and monitoring of fetal response to therapy.

Diagnosis of a significant fetal arrhythmia should result in multidisciplinary planning of timing and location of delivery,[25] balancing potential risks to the mother and fetus with response to therapy. Ideally, fetuses with complex arrhythmias and those associated with SHD should be delivered in centers with expertise in managing these complex cases. Baseline maternal assessment, including history, examination, ECG, and echocardiogram, as indicated, is appropriate prior to prescription of maternal antiarrhythmics for a fetal arrhythmia indication. When administering antiarrhythmic drugs, it is important to monitor the mother to mitigate the risk of potential drug-related side effects, such as excessive QT prolongation; FDA-mandated dosing and precautions should be observed.

Section 3 Overarching principles

In recommendations for the management of all pregnant patients and fetuses with arrhythmias in this document, general principles apply shared decision-making, testing, and treatment, including the composition of the optimal medical care team, defined as the cardio-obstetrics team (see Section 3.2).[30] The cardio-obstetrics team is ideally composed of maternal-fetal medicine subspecialists, electrophysiologists, and fetal or pediatric cardiologists/electrophysiologists, with the addition of anesthesiologists and neonatologists close to the time of delivery.[30] It should be emphasized that recommendations will be applied in the context of the available resources and facilities at a given institution.

3.1. General electrophysiological management

Recommendations for general electrophysiological management

COR	LOE	Recommendations	References
1	C-EO	1. In pregnant patients with cardiac arrhythmias, treatment should be maintained during the pregnancy, delivery, and postpartum periods, preferably using drugs with the longest record of safe use and efficacy in pregnancy, at the lowest effective dose possible, and with periodic reevaluation for continued need for medications.	
1	C-EO	2. In pregnant patients with cardiac arrhythmias, the use and management of antiarrhythmic drugs should be informed by precautions provided by regulatory drug agencies, awareness of potential drug interactions, and knowledge of potential risk to the fetus.	

Synopsis

Treatment of pregnant patients affects both the mother and fetus. Certain principles must be considered in the treatment of pregnant patients to maximize benefits to the mother while minimizing the risk to the fetus. Every pregnant woman with an arrhythmia will face a decision about taking medicines or undergoing other treatment modalities, either during pregnancy or in the postpartum period. However, not all medicines or procedures are safe during pregnancy. Some medicines and other treatment modalities have potential to cause birth defects, pregnancy loss, prematurity, infant death, or developmental disabilities.[21,137,138]

Recommendation-specific supportive text

1. In general, the approach to the evaluation of arrhythmias in the pregnant patient is similar to that in patients who are not pregnant, as a primary goal is to optimize treatment for the mother without compromising fetal safety.[21,137,138] However, when deciding on the best and most appropriate therapy, factors to consider that are unique to the state of pregnancy include the physiological changes that accompany pregnancy; the effect of medications and other therapy on placental blood flow and breastfeeding; and the effects of medications and other therapy on the developing fetus, particularly during the first trimester. Generally, while data are scant on the use of antiarrhythmic drugs in pregnancy, a number of drugs have been used effectively and safely. In fact, very few drugs are contraindicated in pregnancy, and many are also compatible with breastfeeding (Table 5). Periodic reevaluation for continued need, including monitoring of levels and evaluation of the mother and infant for potential side effects, is best practice.[55]
2. If a decision to initiate drug therapy is made by the patient and caregiver, it is important to use the minimal number of drugs at the lowest *effective* dose to reduce drug exposure and potential risks to both the mother and the fetus.[138-140] Ideally, the choice of medication should be limited to those with a history of "reasonable safety profile" during pregnancy. However, as alluded to above, a majority of antiarrhythmic medications fall into the former FDA risk category C for pregnancy, which means that, while adverse effects might have been found in animal studies, there are no well-controlled studies in humans. Nevertheless, if deemed necessary, drugs with limited experience during pregnancy may be administered after weighing risk versus benefit.[141] When administering drugs that have the potential to cause proarrhythmias, FDA-mandated precautions are generally observed as in nonpregnant patients, including adjustments of drug dosing according to changes in physiological conditions such as renal function. Of note, as of June 30, 2015, the FDA has replaced the alphabetic risk categories with the Pregnancy and Lactation Labeling Rule to help physicians better communicate the potential risks and benefits of drugs to patients during pregnancy and lactation. Further details on the Pregnancy and Lactation Labeling Rule are provided in Section 2.3.

3.2. Team-based care and shared decision-making

Similar to other areas of clinical medicine, all treatment decisions result from an informed discussion among the patient and caregivers of potential risks, benefits, and alternatives for treatment.[142] However, treatment decisions for patients who are pregnant are inherently more complex for multiple reasons. First, decisions involve estimates of risks and benefits to both the mother and fetus, which might be divergent. Second, the composition of the care team that estimates risks and benefits is heterogeneous since it includes those who primarily care for 1) people who are pregnant (ie, obstetricians), 2) patients with arrhythmias (ie, electrophysiologists or general cardiologists with expertise in arrhythmias in pregnancy), 3) fetuses and newborns (ie, pediatricians), 4) fetuses and newborns with arrhythmias (ie, pediatric cardiologists or electrophysiologists), and 5) patients with inherited genetic disorders (ie, genetic counselors). Third, patient preferences and decisions are complex as they affect both the mother and fetus. Finally, there is a dearth of high-quality scientific medical data about the safety and efficacy of medication and other treatment modalities in pregnant patients and fetuses.

Recommendations for team-based care and shared decision-making

COR	LOE	Recommendations	References
1	C-EO	1. For the ongoing management and treatment of pregnant patients with cardiac arrhythmias, a cardio-obstetrics team that includes a maternal-fetal medicine subspecialist, a cardiologist and/or electrophysiologist, a pediatric electrophysiologist when fetal arrhythmias are present, an anesthesiologist, and a neonatologist, should be engaged in open communication regarding optimal management strategies, including a birth plan.	
1	C-EO	2. In pregnancies complicated by documented or potential cardiac arrhythmias, shared decision-making that includes discussion of the risks and benefits to both the mother and the fetus of antiarrhythmic drug therapy, specific procedures, and monitoring, as well as the risks of withholding such therapies, is recommended.	
1	C-EO	3. In pregnant patients with complex cardiac arrhythmias, engagement with anesthesiologists and obstetricians to optimize care, including preparations to perform an emergency cesarean delivery if necessary, is recommended when performing invasive electrophysiology procedures.	
1	C-EO	4. In pregnant patients with complex cardiac arrhythmias, consultation with a cardiac electrophysiologist, if available locally, or a cardiologist with expertise in arrhythmias is recommended (preferably with experience with pregnant patients); management at centers with expertise in women with cardiovascular disease is preferable.	

Synopsis

Shared decision-making with the mother and an experienced clinical team with wide expertise using evidence-based data is optimal for improving pregnancy outcomes. The role of the patient as an active participant in the dialog and the importance of all caregiver roles—including nurses, advanced practice providers, genetic counselors, social workers, and physicians—is now emphasized. Modern ideal care models emphasize and promote patients' informed (evidence-based) involvement in decision-making about management and treatment options. Components required for medical shared decision-making are involvement of the patient (and family for pediatrics) and the caregivers, shared information via dialog between all parties, parties taking steps to build a consensus about the preferred treatment, and, finally, agreement being reached on the care plan or treatment for the individual patient.[143]

Recommendation-specific supportive text

1. A coordinated team approach to patient care has been shown to improve outcomes in all areas of medicine. Recent guidance in obstetrics, CHD care, and cardiac resuscitation have included specific recommendations for key team members with the most relevant and important knowledge base.[21,30,144,145] In this consensus statement, the cardio-obstetrics team (see Section 1.10) would ideally be composed of a maternal-fetal medicine subspecialist, an electrophysiologist and/or a cardiologist with expertise in arrhythmias during pregnancy, a pediatric electrophysiologist when fetal arrythmias are present, an anesthesiologist, and a neonatologist.
2. Shared medical decision-making is a process by which clinicians collaboratively help patients reach evidence-informed and value-congruent medical decisions.[143] This process is particularly important in pregnancy, where there can be competing risks and benefits for the pregnant patient and fetus.[14] In the case of pregnancy, there are often disparate potential risks and benefits of testing or treatment on the mother and the fetus, and the absolute value of the potential benefits is determined in large part by the personal values and judgment of the mother. Support for shared decision-making in which women and their care providers discuss risks and benefits of their different options, disclose their preferences, and jointly make a decision is now an expectation in obstetric care.[146] Also, for most women, participation in decision-making during maternity care has been shown to have a positive impact on their childbirth experiences.[147]
3. Obstetricians or maternal-fetal medicine subspecialists and anesthesiologists are among the important cardio-obstetrics team members who care for all pregnant patients who are high risk. Recommendations for the care team members for pregnant patients and fetuses with arrhythmias are therefore similar to other high-risk pregnant patients and fetuses with potentially life-threatening disorders; the care team should include an anesthesiologist and obstetrician who are prepared to contribute care if the need for urgent delivery of the fetus is required.[21,145]
4. Medical science and practice are evolving rapidly toward further subspecialization by practitioners in all fields. The rapid evolution in diagnostic and therapeutic options for cardiac arrhythmia, including new medications and techniques, means that early referral to a cardiac electrophysiologist should be actively considered for management of arrhythmia in pregnant patients.[20,142,148] The use of invasive technologies such as catheter ablation and device implantation can now be performed, when clinically indicated, more effectively and with minimal radiation exposure during pregnancy and can obviate the need for ongoing pharmacological therapies.

3.3. Genetic testing

Recommendation for genetic testing

COR	LOE	Recommendation	References
1	C-LD	**1. In pregnancies complicated by a documented or suspected family history of IAS or arrhythmogenic cardiomyopathy (ACM), clinical cardiac evaluation and genetic counseling with consideration of genetic testing are recommended, ideally provided by an experienced cardiac genetics team.**	149-154

Synopsis

The evaluation and treatment of families with IAS or ACM require a multidisciplinary team approach.[27,28] There are deep and often overwhelming medical and psychosocial implications of an IAS or ACM diagnosis and genetic testing on patients and families. The diagnosis of IAS or ACM and a positive or negative genetic test can raise many questions for the patient and family related to the reliability of testing; risks for sudden cardiac death; transmissibility of disease to future offspring; future participation in athletics; insurability; future employment prohibition; and other important, life-changing topics. Evidence suggests that a structured cardiac genetics team approach improves the diagnosis rate and appropriate care for patients and families with IAS and ACM.[27] Early diagnosis and treatment of newborns with IAS or ACM have the potential to improve patient outcomes.

Recommendation-specific supportive text

1. Early diagnoses and treatment of newborns with a family history of IAS or ACM through clinical evaluation and genetic testing allow for early interventions and potentially reduce the risk of sudden cardiac death. Including a 3-generational maternal and paternal medical history as part of genetic evaluation of offspring born to a parent with an IAS or ACM provides valuable information on the disease and cardiac risk.[10] Genetic testing can also be informative in cases of stillbirths and sudden infant death syndrome, which can be secondary to IAS.[153] Engaging a team of electrophysiologists or cardiologists, specialist nurses, and genetic counselors experienced in cardiovascular genetic diseases is important to address the medical, genetic, and psychological needs of the family.[27,28,149]

Section 4 Procedural considerations for arrhythmia management during pregnancy

The purpose of this section is to provide recommendations on procedural interventions and considerations often required when treating arrhythmias in pregnancy. The interventions discussed in this section are universal in the sense that they can be applied to any number of different arrhythmias and, as such, are not arrhythmia-type specific; for this reason, they are presented at the beginning of this consensus statement.

4.1. Cardioversion during pregnancy

Direct current (or current, or electrical) cardioversion was first performed in the 1950s and is now performed routinely. Cardioversion is aimed primarily at termination of atrial and/or ventricular tachyarrhythmias, typically with the goal of restoring a perfusing (ie, sinus or paced) rhythm that is better tolerated by the patient from a hemodynamic and symptomatic standpoint. Electrical cardioversion or defibrillation can be lifesaving when applied in urgent circumstances and should not be withheld because of concerns of pregnancy or fetal harm. The success rate is increased by accurate tachycardia diagnosis, careful patient selection, adequate electrode (paddles) application, determination of the optimal energy and anesthesia levels, prevention of embolic events and arrhythmia recurrence, and airway conservation, while minimizing possible complications. Potential complications are generally rare and transient, such as bradycardia and superficial skin burns, although serious consequences, such as ventricular fibrillation due to lack of synchronization between the direct current shock and the QRS complex, might occur if cardioversion is performed inappropriately.

Recommendations for cardioversion during pregnancy

COR	LOE	Recommendations	References
1	C-LD	1. In pregnant patients with unstable SVT or VT, direct current synchronized cardioversion or defibrillation is recommended with energy dosing as in the nonpregnant patient.	155
1	C-LD	2. In pregnant patients with stable, symptomatic SVT or VT refractory or with contraindications to pharmacological therapy, elective synchronized cardioversion is recommended with fetal evaluation as indicated by the cardio-obstetrics team.	155-159
1	C-LD	3. In pregnant patients undergoing synchronized cardioversion or defibrillation, electrodes should be placed avoiding breast tissues to optimize current delivery to the heart.	155,160,161

Synopsis

In pregnant patients, the safety and efficacy of cardioversion as a procedure for treating cardiac tachyarrhythmias have been topics of attention in case reports and case series because of concerns about the safety of the procedure and its potential effects on the fetus. Several case reports and case series have shown that this procedure is safe in pregnancy for the treatment of both SVT and VT accompanied by hemodynamic instability, significant symptoms, and/or refractoriness to antiarrhythmic drug therapy.[155,158,162]

Recommendation-specific supportive text

1. In scenarios where there is significant hemodynamic compromise, such as rapid VT or certain unstable forms of SVT, the priority is to restore normal hemodynamics; thus, direct current cardioversion should be performed in pregnant patients following the same resuscitation algorithms as in the general population, without delay out of concern for potential harm to the fetus.[155,162] There is no evidence to support the use of difference shock energy outputs, other than what is already used traditionally to treat SVT or VT in the general population, as transthoracic impedances have been found to not change in a statistically significant manner before and after delivery.[161]
2. Cardioversion is safe and effective during pregnancy. The case reports and case series available in the medical literature have shown no evidence of harm to fetal circulation when umbilical artery indices are evaluated before and after cardioversion procedures performed on pregnant patients.[158] Monitoring of the fetal heart rate is advised once fetal viability is reached, and treatment in facilities that have the capability of performing immediate cesarean deliveries is preferred.

3. Depending on the arrhythmia being treated, defibrillator paddles (or electrode pads) can be placed in different configurations, mainly sterno-apical or antero-posterior. The sterno-apical position (Figure 4A) requires having the sternal paddle or patch electrode placed just to the right of the upper sternal border and below the clavicle, with the apical paddle or electrode placed to the left of the nipple with the center of the electrode in the midaxillary line. This position is generally recommended for treatment of ventricular arrhythmias.[155,161,162] An alternative shock vector, consisting of antero-posterior placement (Figure 4B) of the electrodes or paddles (parasternal and left infrascapular), has been proposed for treatment of atrial arrhythmias, and can be also used following unsuccessful initial attempts with the sterno-apical vector, as the antero-posterior vector may lead to lower transthoracic impedances. In pregnant patients, special attention should be dedicated to avoiding the breast tissue in order to maximize the total current delivery to the heart, as the adipose tissue associated with the breasts, particularly during pregnancy, may contribute to a higher resistance to the actual delivery of electrical current to the heart and theoretically decrease the efficacy of the procedure.[155,160,162]

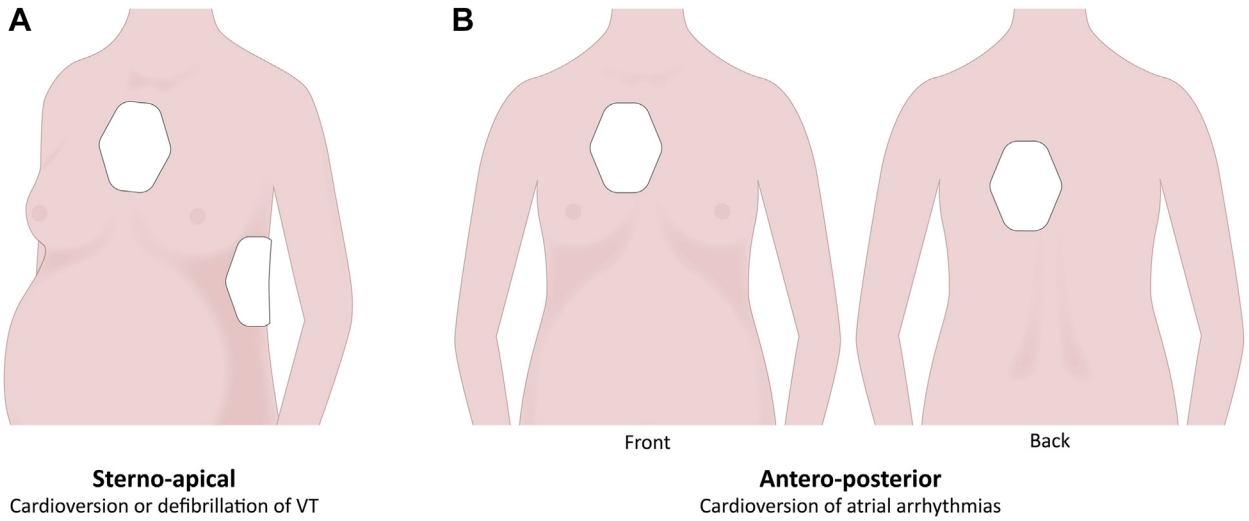

Figure 4 Electrode placement during pregnancy to avoid breast tissue. **A**, sterno-apical electrode placement, which is generally used for cardioversion or defibrillation of ventricular tachycardia (VT). **B**, antero-posterior electrode placement, which is generally used for cardioversion of atrial arrhythmias.

4.2. Radiation exposure during cardiac procedures and hemodynamic concerns related to pregnancy

When arrhythmias occur during pregnancy, an important concern is the potential for adverse maternal and fetal outcomes.[45] As such, therapy should be provided promptly and effectively, with the main goal of restoring normal hemodynamics. When an invasive procedure, such as cardiac ablation, is deemed necessary for managing the arrhythmia, concerns universally arise about the potential risk to the fetus due to radiation exposure. Fortunately, a number of studies suggest that the risk of lifetime malignancy for the fetus from radiation exposure in utero during cardiac procedures is negligible. Furthermore, newer technologies allow for performing cardiac ablations and device implants with minimal or even zero fluoroscopy.

Recommendations for radiation exposure during cardiac procedures and hemodynamic concerns related to pregnancy

COR	LOE	Recommendations	References
1	C-LD	1. In pregnant patients with hemodynamically significant sustained cardiac arrhythmias refractory or with contraindications to pharmacological therapy who are candidates for catheter ablation, the benefit of controlling maternal tachycardia should be prioritized over the potential radiation risks to the fetus, especially if the procedure is done after the first trimester and radiation exposure is minimized to as low as reasonably achievable.	163-165
1	C-LD	2. In pregnant patients undergoing catheter ablation, the use of techniques and technology to minimize radiation exposure to as low as reasonably achievable during the procedure is recommended.	163,164,166
1	C-EO	3. In pregnant patients undergoing high-risk catheter ablation procedures, care by a cardio-obstetrics team prepared to manage potential complications, including urgent delivery if the fetus is close to term, is recommended.	
3: No benefit	C-LD	4. In pregnant patients undergoing cardiac procedures requiring fluoroscopy, placing a pelvic lead apron over the patient is not beneficial because it does not substantially reduce radiation exposure to the fetus.	163

Synopsis

Although invasive cardiac procedures are best avoided during pregnancy, they can be performed safely when necessary, as most cardiovascular interventions, including ablation procedures, are unlikely to exceed the threshold dose for excess lifetime malignancy risk to the fetus. During catheter ablation procedures, modern technology allows for limiting the radiation dose to a minimum, and even zero radiation is possible. Planning of ablation procedures in pregnant patients, in coordination with a cardio-obstetrics team, should include planning for the potential need for urgent delivery, especially with high-risk interventions. The practice of placing a lead apron to shield the pelvis for the purpose of reducing radiation exposure to the fetus appears to offer limited benefit.

Recommendation-specific supportive text

1. Cardiac procedures in pregnant patients are generally avoided because of concerns that radiation may expose the fetus to an increased risk of malignancy and congenital malformations. However, the fetal radiation dose for most common cardiovascular interventions is not likely to exceed the 50 mGy negligible-risk threshold dose for excess malignancy.[165] Damilakis et al[163] studied radiation dose to the fetus in 20 women undergoing ablation procedures for SVT, using an anthropomorphic, realistic human-like model to simulate pregnancy. They estimated that radiation exposure during a typical SVT ablation procedure was well below the threshold of long-term risk of malignancy.[163] Furthermore, Damilakis et al[163] used traditional fluoroscopy, but technological advances, such as 3D mapping systems, allow ablation procedures to be done safely with minimal or no fluoroscopy.[164]
2. Szumowski et al[164] reported their experience in 9 pregnant patients undergoing ablation procedures for drug-refractory SVT, ranging from 12 to 38 weeks of gestation. Three women had an electroanatomic map and ablation performed without X-ray exposure, whereas the mean fluoroscopy time in the whole group was 42 ± 37 seconds. Zero fluoroscopy has been increasingly used as well, even for more complex ablation procedures using 3D/electroanatomical mapping.[166] In addition, since the conceptus dose rate is dependent on the conceptus distance from the source (in this case, the heart) during the first trimester, Damilakis et al[163] reported that fluoroscopic imaging with an empty bladder delivered the lowest dose to the conceptus.
3. In a pregnant patient in whom an ablation procedure is deemed necessary, the potential risk to the mother and fetus can vary greatly according to the severity and type of arrhythmia, the hemodynamic consequences, the complexity of the ablation procedure, and the underlying cardiovascular substrate. It is therefore optimal that the pregnant patient is cared for by a cardio-obstetrics team (see Sections 1.10 and 3.2) prepared ahead of time to intervene in the case of complications, especially in high-risk cases, such as ablation of refractory VT, and in the event that urgent delivery is required.
4. Damilakis et al[163] estimated radiation doses for a potential conceptus by using dose data obtained via an anthropomorphic, realistic human-like model simulating pregnancy at the first, second, and third trimesters in 20 women of childbearing age undergoing ablation procedures. Additional dose measurements were carried out with the abdomen and pelvis of the phantom shielded with 0.5 mm thick lead aprons, to investigate the effect of external shielding on conceptus dose. The authors concluded the dose of radiation the conceptus was exposed to with lead shielding was just 3% lower than that without shielding for all periods of gestation. This was explained by the fact that most of the conceptus radiation exposure came from scatter from the thorax of the mother, not directly from the beam. Furthermore, there is the possibility that under real-world scenarios, the presence of lead in the field of the radiation beam increases radiation output, and, as a result, there is more scattered radiation to the fetus.[163] Thus, the use of a lead apron over the pelvis is unlikely to substantially reduce radiation exposure to the fetus.

4.3. Anesthesia considerations

Pregnant patients with cardiac arrhythmias may require anesthesia for treatment and for peripartum management. Anesthesia necessitates accommodation for a number of physiological changes observed during pregnancy. For example, there is an increased oxygen consumption with a tendency to desaturate due to changes in lung volumes leading to decreased residual volume caused by the rising uterus. Shunting also increases in the third trimester. Also, the laryngeal and pharyngeal landmarks change with anterior displacement of the trachea. Engorgement of the airway requires a smaller endotracheal tube (±7.0 mm). Thus, the pregnant airway is difficult to manage, and specific expertise and experience are required. For induction of general anesthesia during pregnancy, rapid sequence is used to prevent aspiration. Cricoid pressure is no longer favored since there is minimal evidence to support its benefit. Accommodation for aortocaval compression warrants left lateral tilt to optimize maternal hemodynamics. Relaxation of gastroesophageal sphincter and prolonged intestinal transit time increase risk of aspiration due to abundance of progesterone.

Recommendations for anesthesia considerations			
COR	LOE	Recommendations	References
1	C-LD	**1. In pregnant patients with arrhythmias associated with hemodynamic instability requiring cardiac interventions, general anesthesia is recommended in preference to regional anesthesia for the sake of a secure airway and improved oxygenation during hemodynamic instability.**	167,168
1	C-LD	**2. In pregnant patients undergoing cardiac procedures to manage maternal arrhythmias later in gestation (beyond 26 weeks), left lateral tilt positioning is recommended as feasible to minimize aortocaval compression and optimize maternal hemodynamics around and during the time of the procedure.**	167,169
1	C-LD	**3. In pregnant patients undergoing cardiac procedures to manage maternal arrhythmias, medications used for anesthesia should be reviewed and modified, when possible, to prevent exacerbation of underlying maternal arrhythmogenic conditions.**	169,170
1	C-EO	**4. In pregnant patients with arrhythmias associated with hemodynamic instability requiring operative and/or nonoperative cardiac interventions, intraprocedural monitoring of the viable fetus is recommended, in consultation with the cardio-obstetrics team, to manage potential complications including urgent delivery.**	

Synopsis

Pregnant patients with arrhythmias may require anesthesia in the peripartum period or when undergoing interventions required for the treatment of their arrhythmias. Anesthesia performed during pregnancy requires modifications that accommodate the physiological changes of pregnancy, particularly regarding airway management. Aortocaval compression, which decreases venous return and increases cardiac afterload, diminishes maternal cardiac output, which can compromise both maternal and fetal status. Uterine tilt or uterine displacement can ameliorate this hemodynamic perturbation during anesthesia for pregnant patients with arrhythmias. Intraoperative or intraprocedural fetal monitoring can be used for pregnant patients with arrhythmias receiving anesthesia to optimize fetal status. However, failure of corrective measures to reduce hemodynamic instability that affect uterine blood flow may require delivery by a cardio-obstetrics team. Modification of medications used throughout the anesthesia process may be required in patients with susceptible arrhythmogenic substrates, such as LQTS.

Recommendation-specific supportive text

1. Sustained arrhythmias during pregnancy increase the risk of hemodynamic instability. Although regional anesthesia is generally preferred during pregnancy to avoid more difficult airway management and, theoretically, to optimize fetal/neonatal risks,[171] general anesthesia for cardiac procedures will optimize oxygenation during hemodynamic instability. When general anesthesia is planned, expertise in safe obstetric general anesthetic administration is optimal.[172]
2. Aortocaval compression occurs as a result of the enlarging uteroplacental unit as early as the second trimester of pregnancy.[173,174] More contemporary cardiac MRI data corroborate this pregnancy phenomenon, demonstrating improvement in cardiac function with the left lateral tilt of 30 degrees, compared with parameters obtained in the supine position.[52] If the supine position of the thorax is preferred or required to facilitate interventions, left lateral manual uterine displacement can be performed.[175]
3. Medications used throughout the anesthesia process may exacerbate the arrhythmogenic potential of the underlying substrate, such as prolongation of the QT interval.[169,170] Modification of premedications, induction agents, inhalational agents, neuromuscular blocking, and reversal agents is required. For some drugs, such as atropine, the data are conflicting. See Table 6 for a list of QT-prolonging drugs commonly used in anesthesia. For an extensive list of QT-prolonging drugs, refer to https://crediblemeds.org.
4. Operative and nonoperative interventions aimed at treating arrhythmias may be accompanied by maternal hemodynamic instability that may exacerbate uteroplacental insufficiency in the viable fetus, leading to abnormal fetal heart rate patterns reflective of fetal hypoxia and or fetal acidosis. Corrective measures should be implemented by the anesthesia team members geared toward improving and restoring fetal well-being. Persistent abnormal fetal heart rate patterns may require urgent cesarean delivery necessitating the presence of a cardio-obstetrics team.[176]

Table 6 Perioperative medications that prolong the QT interval[177,178]

Pharmacology class	Medications
Antiemetics	Ondansetron, droperidol
Antihypertensive agents	Nicardipine
Antibiotics	Quinolones, macrolides
Antihistamines	
H1 blocker	Terfenadine, diphenhydramine
H2 blocker	Famotidine
Premedication and sedation	Benzodiazepines (except midazolam)
Induction agents	Ketamine, thiopental
Inhalational anesthetics	Sevoflurane, desflurane, enflurane, halothane, isoflurane
Neuromuscular blocking agents	Pancuronium, succinylcholine
Neuromuscular blocking reversal agents	Edrophonium, neostigmine, glycopyrrolate
Opioids	Methadone, sufentanil
Sympathomimetics	Epinephrine, norepinephrine, dobutamine, dopamine, isoproterenol

4.4. Delivery and lactation

The benefits of breastfeeding cannot be overstated. Human milk provides an optimal amount of micro- and macronutrients for the newborn with both immunologic and antibacterial properties. Breastfeeding favors maternal–infant bonding and is associated with decreased postpartum weight retention. Long term, exclusively breastfed infants commonly have optimal growth and development, decreased incidence of acute and chronic diseases, and fewer developmental and psychological disorders. Breastfeeding should be encouraged in the absence of medical contraindications.

Recommendations for delivery and lactation

COR	LOE	Recommendations	References
1	C-LD	**1. In pregnant patients with cardiac arrhythmias, the route of delivery (vaginal or cesarean) should be determined by the birth plan and obstetrical factors in accordance with best clinical practice, along with continuation of antiarrhythmic drug therapy.**	179
1	C-LD	**2. Pregnant patients receiving antiarrhythmic drug therapy or at risk of cardiac arrhythmias should receive adequate pain control during labor, ideally with the use of neuraxial anesthesia (epidural), to avoid pain-induced catecholamine surges that may trigger preexisting arrhythmias.**	180
1	C-LD	**3. In breastfeeding patients, antiarrhythmic drug therapy should be used when clinically indicated, with a preference for agents with the best safety profile during lactation.**	181-192
1	C-LD	**4. In breastfeeding patients with life-threatening cardiac arrhythmias refractory or with contraindications to other treatment, the decision to treat with amiodarone should balance the severity of the arrhythmia against the potential risk for long-term toxicity with consideration of the risks and benefits of breast milk compared with alternatives such as infant formula or donated breast milk.**	183,191

Synopsis

The available evidence on the safety of antiarrhythmic agents during lactation is limited to case reports and small case series. Overall, most of the commonly used agents in clinical practice appear to pose minimal harm when used while breastfeeding. Given the overwhelming evidence on the benefits of breastfeeding (for both the mother and the neonate), in most cases, continuing lactation will outweigh any theoretical risks associated with medication exposure. In all cases, extensive counseling is recommended with a detailed discussion of the risk-benefit ratio for each individual case. The safety of antiarrhythmic drugs is outlined in Table 5. The route of delivery, vaginal or cesarean, is generally determined by obstetric considerations rather than the maternal arrhythmia. Pain management during labor in patients at risk of arrhythmic complications or receiving antiarrhythmic therapy is important to prevent triggering maternal arrhythmias.

Recommendation-specific supportive text

1. In the vast majority of cases, route of delivery is dictated by obstetrical factors rather than the maternal arrhythmia. A recent study that included 276 pregnant patients with a

large variety of cardiac diseases, including 11.2% of the cohort with arrhythmias, showed no difference in outcomes among women who delivered vaginally versus by elective cesarean section.[179] Similarly, data from ROPAC show no advantage of planned-cesarean over vaginal delivery.[193] Importantly, there is no reason to discontinue antiarrhythmic therapy during the delivery process.

2. Early adequate pain control is of paramount importance, as certain arrhythmias may be potentiated by increased sympathetic activity secondary to pain.[180] Heightened sympathetic tone can lead to increased incidence of arrhythmias, such as in LQTS and catecholaminergic polymorphic ventricular tachycardia (CPVT),[177] or arrhythmias due to increased automaticity. Furthermore, conduction in the AV node is enhanced with increased sympathetic tone, which could potentially exacerbate AV node–dependent arrhythmias. Although the data are limited, 1 study demonstrated a decrease in arrhythmic events using epidural anesthesia compared with no anesthesia.[194]
3. When antiarrhythmics are used during breastfeeding, the risk-benefit ratio must be evaluated in all cases. Agents that pose minimal risk for breastfed infants include digoxin, propranolol, metoprolol, and verapamil.[181,184,188,192] Agents with a favorable safety profile during breastfeeding, albeit with limited available evidence, include carvedilol, esmolol, procainamide, diltiazem, flecainide, and sotalol.[182,185,186,189,190] Amiodarone should be avoided during breastfeeding if possible; however, it may be used if clinically the benefit is thought to outweigh the risks. No data exist on the use of dronedarone or ibutilide; neither is recommended during breastfeeding. In all cases, it is important to educate parents about potential signs of toxicity in infants. Primary care providers involved in the infant's care also need to be educated about potential side effects of the specific antiarrhythmic that is being used during breastfeeding. In very selected cases, evaluation of an infant's serum levels may be required (eg, high doses of flecainide). More information on drugs and breastfeeding can be found in the Drugs and Lactation Database (LactMed; https://www.ncbi.nlm.nih.gov/books/NBK501922).
4. During pregnancy, amiodarone is generally considered a last resort option in the setting of life-threatening arrhythmias. During breastfeeding, the infant receives just a fraction of the mother's weight-adjusted dose, although the precise amount is unpredictable with a median dose of about 11%.[195] Therefore, potential fetal adverse effects depend on maternal dose and duration of drug exposure (cumulative dose). When amiodarone is used, the infant is closely monitored with periodic evaluation of thyroid function. Limited exposure is generally safe, but when prolonged therapy is required, patient and physician should engage in shared-decision discussion, balancing risks and benefits, and consider alternatives to breastfeeding, including the use of milk formulas or, if available, donor breast milk.

Section 5 Diagnosis of pregnant patients with palpitations

Palpitations are frequent in pregnancy, but in the majority of patients they are caused by either no or minor arrhythmias. Pregnancy in healthy individuals is associated with an increase in physiological heart rate and with a slight increase in extrasystole burden. Preexisting arrhythmias in patients with an arrhythmogenic substrate may be exacerbated during pregnancy, but first-onset PSVT or another new-onset arrhythmia is uncommon. In recent reports, AF became the most frequent arrhythmia in pregnancy.[37]

Recommendations for the diagnosis of pregnant patients with palpitations

COR	LOE	Recommendations	References
1	B-NR	1. **Pregnant patients presenting with modest sinus tachycardia or extrasystoles, with an otherwise normal initial evaluation and without suspicion of underlying cardiopulmonary disease, should be reassured without additional testing.**	33,41-43
1	B-NR	2. **Pregnant patients with suspected arrhythmic etiology of unexplained palpitations who have concerning symptoms or suspected electrical or SHD on initial evaluation should undergo ambulatory monitoring as clinically indicated, in consultation with a cardiologist or electrophysiologist with expertise in cardiovascular diseases in pregnancy.**	37,38,41,44-46
1	C-EO	3. **In pregnant patients presenting with palpitations, a detailed history, physical examination, resting 12-lead ECG, and targeted blood testing should be performed at initial evaluation.**	
2a	C-LD	4. **In pregnant patients with suspected arrhythmic etiology of palpitations unexplained after noninvasive cardiac evaluation, especially in the presence of syncope and/or electrical or SHD, consideration of an implantable cardiac monitor (ICM) is reasonable.**	41
3: No benefit	C-EO	5. **In pregnant patients with palpitations in the absence of a documented arrhythmia or other clinical evidence of potential arrhythmogenic substrate, electrophysiological study solely as a first-line diagnostic test should not be performed.**	

Synopsis

In pregnant patients, similar recommendations for diagnostic evaluation of palpitations apply as in nonpregnant patients, with additional consideration given to the increased risks that arrhythmias pose during pregnancy and the radiation risk to the fetus if an electrophysiological study was performed. In general, the diagnostic evaluation rules out the presence of underlying structural or electrical heart disease and ECG documentation during palpitations is performed for symptom–rhythm correlation.[17,19,196] The choice of an arrhythmia monitoring device depends on the frequency of palpitations, with the longer recording duration providing higher diagnostic yield.[17,19,196] Further management testing is specific to the underlying heart disease and type of arrhythmia. The presence of documented arrhythmia in pregnant patients with congenital or acquired heart disease is an important risk factor for adverse maternal and fetal pregnancy outcomes.[16,46] A summary of the approach for the diagnosis of the pregnant patient with arrhythmias is provided in Figure 5.

Recommendation-specific supportive text

1. Pregnancy in healthy individuals is associated with an increase in sinus rhythm frequency and slight increase in extrasystole burden, which return to prepregnancy levels postpartum. In general, resting heart rate increases by 10% or more during pregnancy due to autonomic, hemodynamic, and whole-body volume fluctuations. Patients with extrasystole or sinus tachycardia on ECG documented during ongoing symptoms generally do not benefit from further extensive evaluation. In a study of 110 pregnant patients with structurally normal hearts who were referred for palpitations (87%), dizziness (13%), or syncope (6%), the results of ambulatory Holter monitoring were compared with those for 52 healthy pregnant patients. Sinus tachycardia was found in 9% and 10%, sinus bradycardia in 1% and 2%, atrial extrasystoles in 56% and 58%, and ventricular extrasystoles in 49% and 40% of the group with palpitations without significant difference, compared with the control group, respectively. The mean PVC burden was significantly higher in the symptomatic group than in the control group. However, there was no correlation between arrhythmia frequency and symptoms, as only 10% of symptomatic episodes were accompanied by the presence of any arrhythmia.[33] These findings suggest that palpitation is a frequent symptom in pregnancy and that in the majority of patients it is caused by either no or minor arrhythmias. IST (defined as a resting heart rate >100, a mean ambulatory heart rate >90, and associated symptoms) has been associated with a higher frequency of induction at term, but without impact on maternal or fetal outcomes.[42] Further, pregnancy is a common inciting event for IST, with about 8% of IST patients identifying pregnancy as the inciting event; however, aside from symptoms, IST has not been associated with negative long-term outcomes.[43] That being said, some instances of high-burden PVCs may represent serious arrhythmias or cardiomyopathy. Similarly, persistent fast sinus tachycardia rates may indicate underlying disease processes that require further evaluation.
2. Similar to evaluation of nonpregnant patients, the evaluation of pregnant patients with unexplained palpitations of suspected arrhythmic origin aims at ECG correlation with symptoms. The type of arrhythmia monitoring device that is most diagnostic depends on the frequency of palpitations; longer duration of recording has higher diagnostic yield.[17,19,196] In a recent study of 96 pregnant patients referred for ambulatory 24-hour Holter or external event loop recorder, 76% of the patients had no or benign arrhythmia and 24% had more severe arrhythmia; most frequently SVT and rarely AF or VT were documented.[41] The loop monitor had a higher diagnostic yield. The history of arrhythmia prior to pregnancy predicted a higher likelihood of recurrent arrhythmia during pregnancy.[41] Unexplained palpitations in pregnant patients with a history of congenital or SHD require thorough investigation of the status of the SHD and more aggressive attempts at arrhythmia documentation and diagnosis, to allow for the timely initiation of disease and arrhythmia-specific treatment.
3. The evidence supporting the value of detailed history, physical examination, and resting 12-lead ECG in nonpregnant patients presenting with palpitations and/or supraventricular arrhythmias has been recently reviewed in the *2015 ACC/AHA/HRS Guideline for the Management of Adult Patients with Supraventricular Tachycardia*[19]; the *2019 ESC Guidelines for the Management of Patients with Supraventricular Tachycardia*[8]; the 2017 EHRA *Consensus Document on the Management of Supraventricular Arrhythmias*[17]; and the 2011 EHRA position paper, *Management of Patients with Palpitations.*[196] Although specific studies do not exist and pregnancy is frequently an exclusion criterion, especially in invasive studies of arrhythmias, similar recommendations for diagnostic evaluation of palpitations apply as in nonpregnant patients. In general, the initial evaluation should aim at ruling out potentially life-threatening arrhythmic etiology, ECG documentation of symptoms for specific arrhythmia diagnosis, and evaluation of the presence of underlying structural or electrical heart disease. Specifically, in pregnancy, targeted blood testing can exclude anemia due to bleeding, thyroid dysfunction, infection, electrolyte abnormalities, and other underlying medical conditions that can cause physiological tachycardia or ectopy. ECG documentation during ongoing palpitations will allow clear diagnosis of the type of arrhythmia (Figure 5).

4. Similar to nonpregnant patients, in cases when an arrhythmic origin of palpitation or syncope is strongly suspected based on the history but noninvasive ambulatory monitoring is nondiagnostic, especially when high-risk features are present (such as congenital or acquired structural or electrical heart disease or associated syncope), the insertion of an ICM allows for long-term monitoring and provides increased diagnostic yield in cases of sporadic arrhythmias.[16,196]
5. The adverse effects of radiation exposure to the fetus are discussed in Section 4.2. Electrophysiological study for diagnostic purposes in the absence of a documented arrhythmia or evidence of a potential arrhythmogenic substrate would be very low yield, since in most cases the etiology of palpitations is either no or a minor arrhythmia.[19,33,37,41] In addition to the lack of demonstrated benefit, the risks associated with unnecessary interventions could be harmful.

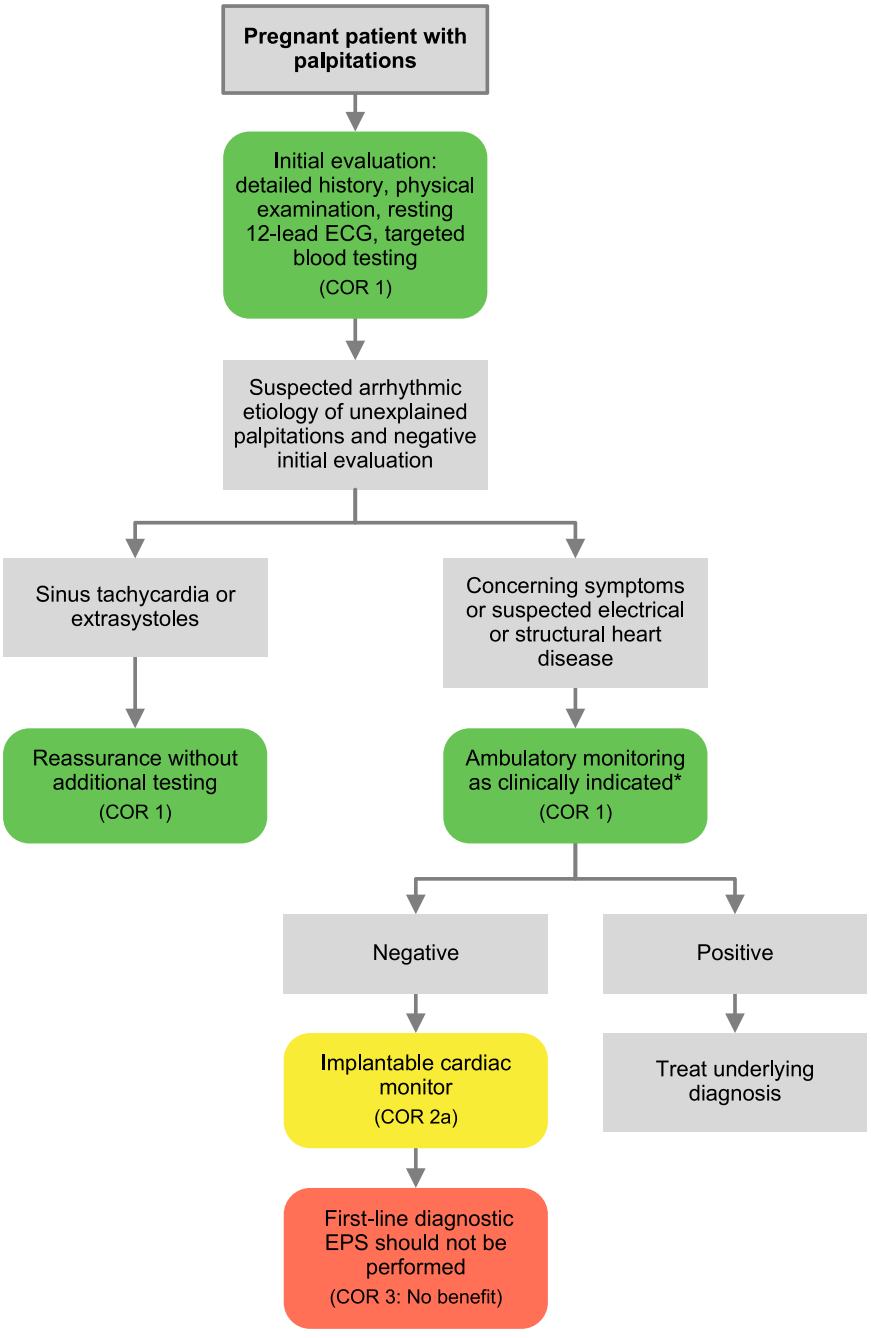

Figure 5 Algorithm showing the approach to the diagnosis of pregnant patients presenting with palpitations. Colors correspond to class of recommendation (COR) in Table 1. *In consultation with a cardiologist or electrophysiologist with expertise in cardiovascular diseases in pregnancy. ECG = electrocardiogram, EPS = electrophysiological study.

Section 6 Diagnosis and management of pregnant patients with syncope

Syncope is a sudden, transient loss of consciousness as a result of global cerebral hypoperfusion.[197] Hemodynamic changes of pregnancy, especially the reduced systemic vascular resistance, may predispose pregnant patients to syncope. The incidence of syncope in pregnancy is about 1%. Moreover, pregnant patients who experience syncope in the first trimester have an increased risk of adverse maternal-fetal outcomes, including recurrent syncope during pregnancy.[47] In general, workup and management of syncope in pregnant patients is similar to that for their nonpregnant counterparts.[18] The most common types of syncope in pregnancy are neurocardiogenic and/or positional syncope, also known as supine hypotensive syndrome. In supine hypotensive syndrome, syncope occurs because of aortocaval compression while in the supine position, and syncope often is accompanied by tachycardia, sweating, and nausea. In this condition, the cause of syncope is anatomic and positional. Orthostatic hypotension is also common, particularly in late pregnancy.[198] While supine hypotensive syndrome is most often due to compression of the inferior vena cava and resulting decrease in blood return to the heart, orthostatic hypotension may be due to relative vasodilation, hypovolemia, or autonomic dysfunction.

6.1. Diagnosis and approach to the pregnant patient with syncope

Recommendations for the diagnosis and approach to the pregnant patient with syncope

COR	LOE	Recommendations	References
1	B-NR	1. In pregnant patients presenting with syncope, a detailed history, physical examination (including orthostatic vitals), resting 12-lead ECG, and targeted blood testing should be performed at initial evaluation.	199-204
1	B-NR	2. Pregnant patients with new onset of unexplained syncope, especially if it occurs in the first trimester or recurs during pregnancy, are at higher risk of adverse pregnancy outcomes and should receive enhanced evaluation, including echocardiogram, followed by close periodic monitoring.	47,205
1	B-NR	3. Pregnant patients with syncope suspected to be of cardiac origin and/or due to suspected cardiovascular abnormalities after initial evaluation should undergo additional cardiac testing, including imaging, as clinically indicated in consultation with a cardiologist or electrophysiologist with expertise in cardiovascular diseases in pregnancy.	206-208
1	C-LD	4. In pregnant patients with recurrent syncope unexplained after comprehensive noninvasive evaluation, including external monitor, insertion of an ICM is recommended.	209-212
3: No benefit	B-NR	5. In pregnant patients presenting with clinical characteristics typical for reflex-mediated vasovagal syncope, a normal physical examination, and a normal resting 12-lead ECG at initial evaluation, further testing is not beneficial.	198,205,213-215
3: No benefit	C-LD	6. In pregnant patients with unexplained syncope but without evidence of cardiac disease or conduction system disease, diagnostic electrophysiological study is not indicated.	216-218

Synopsis

The evaluation of pregnant patients with unexplained syncope requires a systematic approach. Initial evaluation should consist of a comprehensive history and physical exam. A 12-lead ECG is also recommended during initial evaluation. Based on these factors, if the episodes are classic for reflex-mediated vasovagal syncope and physical exam and ECG are normal, no further evaluation is recommended. Otherwise, however, additional evaluations, including echocardiography, expert consultation, and long-term monitoring, are useful adjuncts. The use of electrophysiology studies in the absence of a compelling indication (such as conduction disease on baseline ECG or longer-term monitoring or SHD on echocardiography) is not recommended because of potential for harm related to radiation exposure to the fetus.

An algorithm of the recommendations for the diagnosis of pregnant patients with syncope is provided in Figure 6.

Recommendation-specific supportive text

1. The evidence supporting the value of detailed history, physical examination, targeted blood testing, and resting 12-lead ECG in nonpregnant patients presenting with syncope has been recently reviewed in the *2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients with Syncope*[18] and in the *2018 ESC Guidelines for the Diagnosis and Management of Syncope.*[13] In pregnant patients, although specific studies do not exist and pregnancy is a frequent exclusion criterion in clinical studies, similar recommendations for diagnostic evalua-

tion of syncope apply as in nonpregnant patients, including initial comprehensive history, 12-lead ECG, and physical exam, to elucidate details surrounding the syncopal event and to identify any objective findings suggestive of electrical or other cardiac abnormalities. Basic blood tests, including a complete blood count and electrolytes, are also useful. Other blood tests, such as thyroid function studies or cardiac enzymes, should be ordered based on the clinical context (eg, in the presence of exertional chest pain associated with syncope, or with symptoms suggestive of another disease process).

2. In a recent Canadian retrospective, population-based cohort study of close to 500,000 live births between 2005 and 2014, the overall incidence of syncope during pregnancy was 1% (9.7 per 1000 pregnancies).[47] In this study, the rate of preterm birth was higher in pregnancies with syncope occurring during the first trimester than in pregnancies with syncope in the second and third trimesters (18%, vs 16% and 14% respectively, $P < 0.01$). In this series, 8% of pregnancies had >1 episode of syncope. Also, the rate of congenital anomalies among children born from women with >1 syncope was higher (4.9%) than in those without syncope (2.9%, $P < 0.01$). The rate of arrhythmias and syncope within 1 year postpartum was higher in those with syncope while pregnant than in those without syncope.[47] These findings suggest that pregnant patients with syncope in the first trimester or multiple syncope episodes during the pregnancy are at higher risk of adverse events. In these instances, echocardiogram can rule out the presence of SHD and prolonged cardiac monitoring may be necessary.
3. In cases in which history, examination, and ECG either do not support a clear vasovagal cause or may indicate another cause, further evaluation including echocardiography, tilt table or other autonomic testing, or cardiac MRI should be done as clinically indicated. Consultation with a cardiologist with expertise in pregnancy can ensure safety of the choice of testing and provide the pregnant patient with information on potential fetal risk. Echocardiography has been shown to be normal or nonrelevant in patients with a negative cardiac history and a normal ECG, but in those with a positive cardiac history or an abnormal ECG, relevant cardiac findings may be identified in as many as 27% of patients.[207] Generally, most additional testing beyond an ECG impacts diagnosis or management in fewer than 5% of cases and determines an etiology in fewer than 2%.[219] In general, MRI is preferred to computed tomography scan in pregnancy because of radiation concerns if more advanced cardiac imaging is required. Given the potential patient-specific risks, we recommend consultation with a cardiologist with expertise in managing pregnant patients.
4. ICMs have demonstrated benefit in elucidating a cause of syncope in otherwise undiagnosed cases. Linzer et al[210] reported that the diagnostic yield of ICMs recording was as high as 25% in patients with undiagnosed causes of syncope. Similarly, Sivakumaran et al[211] demonstrated that the probability of obtaining symptom–rhythm correlation was 56% for ICMs vs 22% for Holter monitors. Krahn et al[209] demonstrated that prolonged monitoring strategies with ICMs are more likely to provide a diagnosis than conventional testing, including Holter or external-event monitors, in patients with unexplained syncope. Sliwa et al[212] also showed that ICMs were more effective than 24-hour Holter monitoring in detecting arrhythmias and were safe for pregnant patients.
5. The most frequent etiology of syncope during pregnancy by far is reflex-mediated vasovagal syncope, which can be diagnosed at initial evaluation. The majority of patients have a history of vasovagal syncope episodes prior to pregnancy with typical triggers and prodrome[213,215] and continue to have episodes in the postnatal period.[205] Longer duration of standing or in very rare cases sitting up from supine position,[198] hypovolemia due to bleeding or vomiting (hyperemesis gravidarum), and warm environment may exacerbate symptoms. As in nonpregnant patients, initial evaluation with the detailed history is diagnostic for typical reflex-mediated vasovagal syncope during pregnancy. Reflex-mediated syncope is generally associated with favorable prognosis.[213] There is only 1 case reported of fetal hypoxia due to very prolonged hypotension.[214] Thus, when the history is suggestive of reflex-mediated vasovagal syncope and there are no other compelling findings from physical examination, ECG, or blood testing to suggest another disease process, no further evaluation is necessary, and the provider can reassure the patient this type of syncope is generally benign.
6. The adverse effects of radiation exposure to the fetus are discussed in Section 4.2. Thus, procedures that require fluoroscopic/radiation exposure are potentially harmful to the developing fetus and ought to be avoided unless they are of clear value to optimize treatment for the mother.[216,218] There is a direct correlation between the presence of ECG abnormalities and the likelihood of relevant findings on an electrophysiology study, with an overall low likelihood of electrophysiology study–related abnormalities in the setting of an otherwise normal ECG.[217]

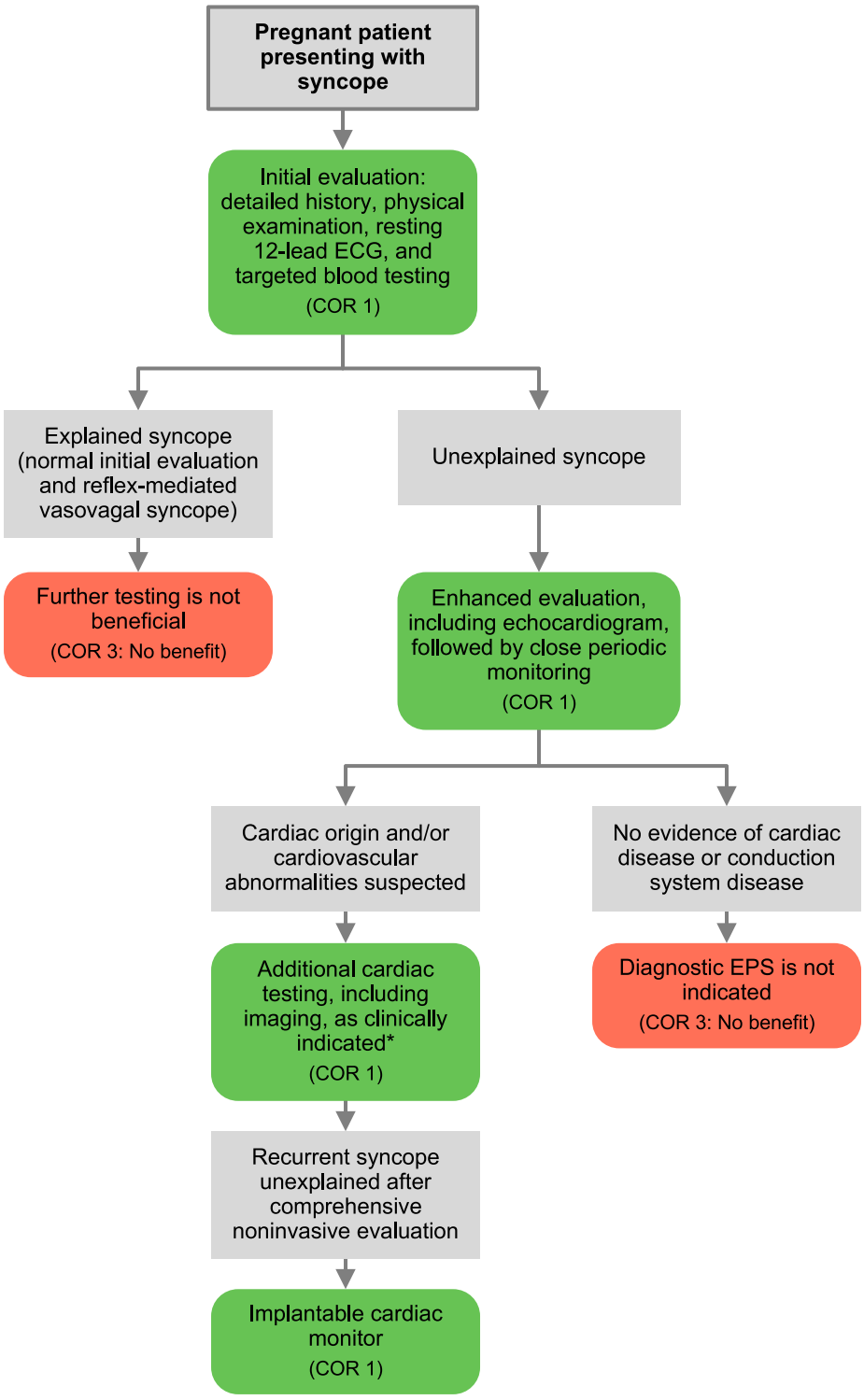

Figure 6 Diagnosis of pregnant patients presenting with syncope. Colors correspond to class of recommendation (COR) in Table 1. *In consultation with a cardiologist or electrophysiologist with expertise in cardiovascular diseases in pregnancy. ECG = electrocardiogram, EPS = electrophysiology study.

6.2. Management of syncope and orthostatic hypotension in the pregnant patient

Recommendations for management of syncope and orthostatic hypotension in the pregnant patient			
COR	LOE	Recommendations	References
1	B-NR	1. In pregnant patients with syncope, therapy should be provided as indicated in the nonpregnant patient.	220
1	B-NR	2. In pregnant patients with syncope presumed to be due to supine hypotensive syndrome, left lateral decubitus position and adequate hydration are recommended.	221,222

Synopsis

Once the cause of syncope in the pregnant patient has been determined based on comprehensive evaluation, management should be as indicated for nonpregnant patients with consideration of the health of both the mother and the fetus in the treatment strategy. In the pregnant patient, a specific consideration, in addition to standard causes of syncope, is supine hypotensive syndrome, which is anatomic and positional.

Recommendation-specific supportive text

1. Syncope is common in pregnancy due to decreased venous return and cardiac output. These physiological changes may lead to new presentations of common causes of syncope that may be seen in the nonpregnant patient. Vasovagal syncope is the most common type of syncope. Syncope in the pregnant patient is managed as indicated in the nonpregnant patient. First-line therapy consists of conservative measures such as increasing salt and water intake, using compression garments, and avoiding triggers like rapid positional changes from lying or sitting to standing. After the first trimester, increased salt intake and fludrocortisone have been shown to be beneficial in refractory cases.[223] Ultimately, it is still important to consider the type of workup and treatment strategy in light of the health of both the mother and the fetus. Thus, a multidisciplinary discussion among a maternal-fetal medicine subspecialist, electrophysiologist, and anesthesiologist is highly encouraged.[12,18]
2. In a study from the United Kingdom, investigators evaluated the hemodynamic impact of the degree of lateral tilt in 32 women in late third trimester. Stroke volume and cardiac output were highest with complete left lateral tilt with 17% decrease when on the right side.[221] Others have confirmed a decrease in cardiac output in supine position later in pregnancy due to caval and aortic compression.[224]

Section 7 Management of specific arrhythmias during pregnancy

Atrial arrhythmias, such as PACs and SVT, are the most common cardiac arrhythmias to present during pregnancy. The prevalence of SVT has been estimated at 24 per 100,000 pregnancy-related hospitalizations.[38] Some patients have a history of palpitations or SVT, while others present for the first time during pregnancy. SVT can be secondary to AV node reentry or an accessory pathway, either overt or concealed. Most women with SVT present with symptoms of palpitations during pregnancy, but some present with presyncope, syncope, dyspnea, or chest pain. Palpitations are described as rapid regular heartbeats and have an abrupt onset. SVT occurs most commonly in the second or third trimester. The incidence of AF or AFL is low in pregnant patients without SHD (59.3 per 100,000 pregnancies).[225] ROPAC showed that the incidence of AF during pregnancy in patients with SHD was 1.3%.[226] This section covers maternal arrhythmias that are not related to IAS, which are covered in Section 12.1.

7.1. Management of atrial ectopy and supraventricular tachycardia during pregnancy

7.1.1. Management of acute supraventricular tachycardia during pregnancy

Recommendations for the management of acute supraventricular tachycardia during pregnancy			
COR	LOE	Recommendations	References
1	C-LD	1. In pregnant patients with acute onset of SVT, vagal maneuvers are recommended as a first-line therapy for tachycardia termination.	38,227
1	C-LD	2. In hemodynamically stable pregnant patients with acute onset of SVT, intravenous adenosine is recommended as the first-line pharmacological therapy.	38,227
1	C-LD	3. In hemodynamically unstable pregnant patients with acute onset of SVT, synchronized direct current cardioversion is recommended, with energy dosing as in the nonpregnant patient.	38,227
2a	C-LD	4. In hemodynamically stable pregnant patients with acute onset of SVT refractory or with contraindications to adenosine, intravenous beta-blockers, such as metoprolol or propranolol, are reasonable for termination of acute SVT.	38,227
2b	C-LD	5. In hemodynamically stable pregnant patients with acute onset of SVT refractory or with contraindications to adenosine or beta-blockers, intravenous calcium channel blockers, such as verapamil or diltiazem, or intravenous procainamide may be considered.	228-230

Synopsis

An algorithm for the management of acute SVT is provided in Figure 7. The management of acute SVT during pregnancy is similar to management in the nonpregnant population, although some important differences exist. Vagal maneuvers are generally considered first-line intervention, although data specific to pregnancy are scant, so the technique is an extrapolation from the general population. Adenosine, with its favorable safety profile in pregnancy, is the first-line medication option. When additional intravenous nodal blocking agents are needed, intravenous metoprolol or propranolol have the most robust safety. Experience with intravenous calcium channel blockers is less robust, and given the potential for hypotension, these agents are generally used in patients who are refractory or with contraindication to adenosine and beta-blockers. Procainamide and digoxin also remain options in these cases.

Recommendation-specific supportive text

1. SVT may be secondary to atrial tachycardia (AT), AV nodal reentry tachycardia, or AV reciprocating tachycardia, with an accessory pathway either overt or concealed. For both AV nodal reentry tachycardia and AV reciprocating tachycardia, the AV node is a required component of the reentrant circuit, and maneuvers or medications that slow AV conduction can terminate the SVT. Vagal maneuvers, such as the Valsalva maneuver or carotid sinus massage, are simple methods for terminating SVT and are safe to attempt in pregnant patients before resorting to pharmacological therapy.[162] The Valsalva maneuver requires that the patient bear down against a closed glottis for 10 to 30 seconds and is performed with the patient in a supine position.[231,232] Carotid massage is performed by applying pressure over the right or left carotid sinus for 5 to 10 seconds.[231] Carotid auscultation for bruits should be done prior to carotid massage. Ice-cold wet towels on the face or facial immersion in cold water are alternative vagal maneuvers.[233] The practice of applying pressure to the eyeball as a vagal maneuver has been abandoned due to the risk of complications, including damage to the eye, and the existence of other options.[21]
2. SVT can usually be terminated with adenosine, which has been used effectively in pregnant patients.[64,162,234] Side effects such as flushing, shortness of breath, or chest discomfort can occur after administration, but typically resolve quickly due to the short half-life of the drug. Adenosine is given as an intravenous bolus. Continuous ECG monitoring is important during adenosine administration to document rhythm changes.
3. Acute-onset SVT can be associated with hemodynamic instability, including syncope, pulmonary edema, cardiogenic shock, hypotension, and brain hypoperfusion. When acute SVT with hemodynamic instability occurs, it should be treated promptly. Direct current cardioversion is safe during pregnancy and effective for all women with signs of hemodynamic instability.[159] Electrodes should not be applied to the breast tissue (see Section 4.1).[159] The energy dose administered is similar to that in the nonpregnant patient.[21] Fetal monitoring is appropriate after cardioversion, if warranted by concerns about fetal well-being.
4. Although less effective than adenosine, intravenous beta-blockers are an alternative treatment for acute SVT, espe-

cially in hemodynamically stable patients refractory or with contraindications to adenosine.[64,162] Most studies of beta-blocker use during pregnancy use intravenous metoprolol or propranolol. The use of esmolol in pregnancy has not been studied, so this medication is less preferred.

5. There is less experience using intravenous verapamil to treat SVT during pregnancy. Intravenous verapamil can cause significant hypotension and therefore is usually considered only when SVT is refractory to adenosine or beta-blockers, or when there are contraindications to these 2 preferred agents.[64,162] Although intravenous procainamide has been used safely during pregnancy, data on its use in treating acute onset SVT during pregnancy are limited.[64,162] Long-term oral procainamide can be associated with a lupus-like syndrome and is usually avoided if other options are available.[229]

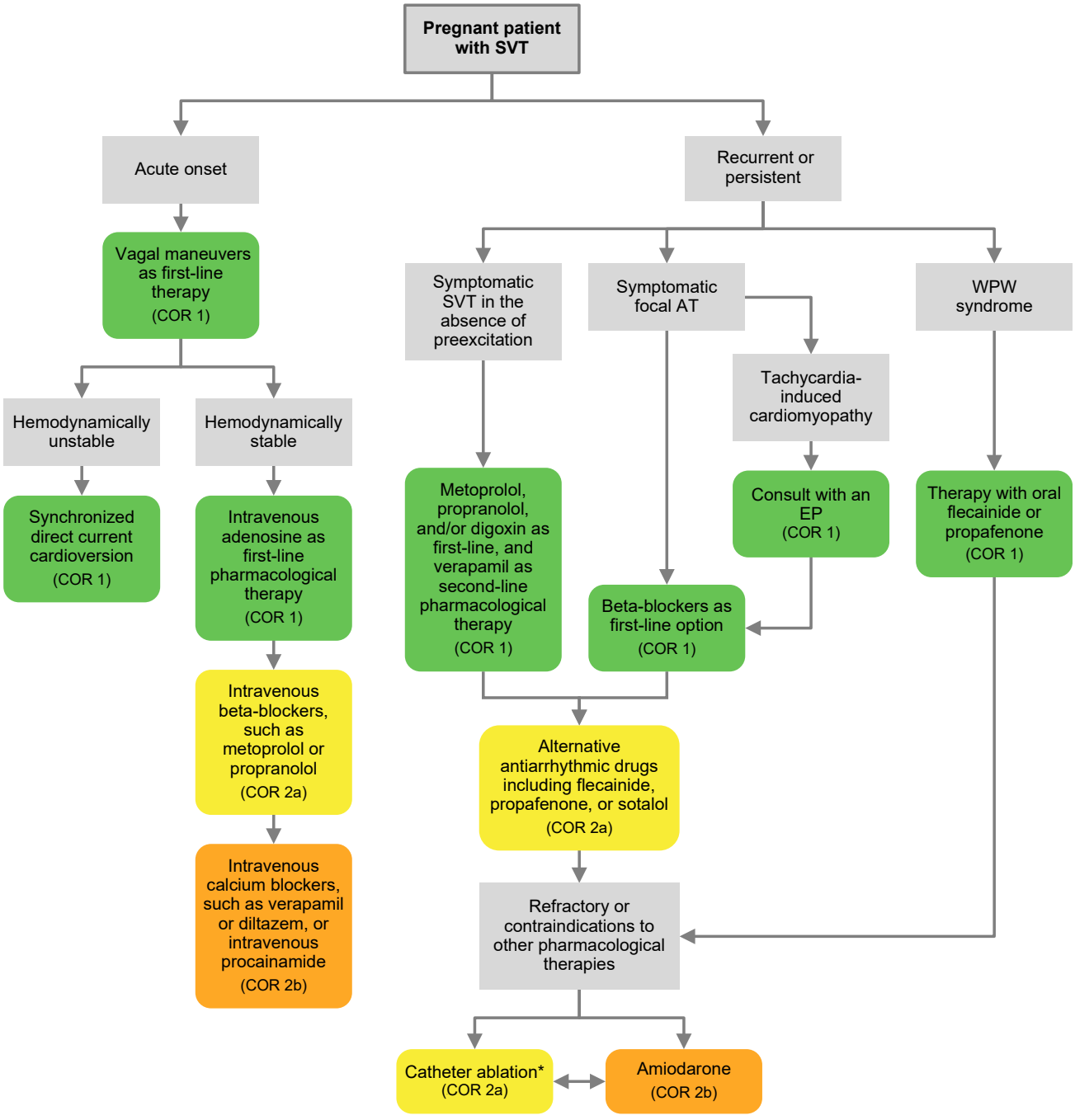

Figure 7 Algorithm of recommendations for the management of pregnant patients with supraventricular tachycardia (SVT). Colors correspond to the class of recommendation (COR) in Table 1. *With attention to and techniques for minimizing radiation exposure to as low as reasonably achievable. AT = atrial tachycardia, EP = electrophysiologist, WPW = Wolff-Parkinson-White.

7.1.2. Management of nonacute atrial ectopy and supraventricular tachycardia during pregnancy

Recommendations for the management of nonacute atrial ectopy and supraventricular tachycardia during pregnancy			
COR	LOE	Recommendations	References
1	B-NR	1. In pregnant patients with PACs and intolerable symptoms, treatment with beta-blockers is recommended, preferably with metoprolol or propranolol.	33,38
1	C-LD	2. In pregnant patients with PACs who either are asymptomatic or have tolerable symptoms, reassurance is recommended with no need for intervention.	33
1	C-LD	3. In pregnant patients with symptomatic SVT in the absence of preexcitation, metoprolol, propranolol, and/or digoxin should be used as first-line options and verapamil as the second-line option for the chronic oral prophylaxis of SVT.	38,227
1	C-LD	4. In pregnant patients with Wolff-Parkinson-White syndrome and poorly tolerated or frequent episodes of SVT, therapy with oral flecainide or propafenone is recommended for the pharmacological management of SVT.	235,236
1	C-LD	5. In pregnant patients with tachycardia-induced cardiomyopathy, aggressive treatment of the tachycardia with beta-blockers as a first-line option and early consultation with an electrophysiologist for escalation of pharmacological therapy and/or ablation are recommended.	237
2a	C-LD	6. In pregnant patients with symptomatic recurrent SVT refractory or with contraindications to digoxin, beta-blockers, or calcium channel blockers, alternative antiarrhythmic drugs, including flecainide, propafenone, or sotalol, are reasonable.	108,238
2a	C-LD	7. In pregnant patients with recurrent SVT refractory or with contraindications to pharmacological therapies, catheter ablation is reasonable with attention to and techniques for eliminating or minimizing radiation exposure to as low as reasonably achievable.	163
2b	C-LD	8. In pregnant patients with poorly tolerated SVT refractory or with contraindications to other pharmacological and interventional therapies, therapy with amiodarone may be considered.	126

Synopsis

The most common arrhythmias during pregnancy are PACs, which generally require no intervention unless highly symptomatic, whereas sustained SVT can negatively impact maternal and fetal health.[45,227] Ideally, patients with SVT who are considering pregnancy will undergo ablation therapy before conception. During pregnancy, SVT can usually be treated with medications.[38] Cardioversion is sometimes necessary and can be performed safely during pregnancy. The treatment of atrial ectopy (Figure 8) and SVT (Figure 7) is based on several factors, including the severity of symptoms, the frequency and duration of the arrhythmia, concurrent cardiac disease (eg, underlying valve dysfunction, left ventricular [LV] systolic dysfunction), and the available treatment options and their effect on the developing fetus or the neonate (via breastfeeding). Drugs with the best safety record in pregnancy are generally first-line options. Catheter ablation procedures can be performed with minimal or zero fluoroscopy, avoiding radiation risk to the fetus. SVTs of all mechanisms, including focal AT, are amenable to ablation. Amiodarone, despite its risks, remains an option in hemodynamically significant refractory cases.

Recommendation-specific supportive text

1. Occasionally, PACs are associated with intolerable symptoms during pregnancy and therapy is necessary. The studies on the treatment of PACs during pregnancy involve a beta-blocker, either metoprolol or propranolol.[64,162,234] Atenolol is best avoided during pregnancy because it is associated with lower birth weight when compared with other agents.
2. PACs are common during pregnancy and are very rarely associated with adverse events in the mother or the fetus.[33] PACs do not require treatment unless symptoms are intolerable for the mother. Avoiding potential precipitating factors, such as caffeine, alcohol, stimulants, and drugs with beta-agonist effects, can decrease the occurrence of PACs.
3. Digoxin, metoprolol, propranolol, and verapamil are not teratogenic and have been used to prevent recurrent symptomatic SVT in pregnant patients.[64] When necessary, the lowest-possible dose of beta-blockers should be used because they are associated with low birth weight, bradycardia, and neonatal hypoglycemia.[62,64] Digoxin, metoprolol, and propranolol have a robust safety record during pregnancy and as such are favored as initial options prior to using calcium channel blockers. Digoxin can be used alone or in combination with beta-blockers and calcium

channel blockers. Atenolol, a former FDA risk category D medication, is better avoided because of the risk of fetal growth restriction. In general, AV nodal blockers are avoided in the presence of ventricular preexcitation.

4. Treatment of SVT in the setting of Wolff-Parkinson-White syndrome is more complex due to the risk for development of preexcited AF. Beta-blockers, verapamil, diltiazem, digoxin, and amiodarone can enhance conduction over the accessory pathway and precipitate an unstable arrhythmia if women develop AF during SVT. Medications such as flecainide and propafenone slow or block conduction over the pathway and prevent preexcited AF. Although experience is limited, flecainide or propafenone can be used for the prevention of SVT episodes in patients with Wolff-Parkinson-White syndrome during pregnancy.[64]
5. Tachycardia-induced cardiomyopathy can occur in pregnant patients, often as a consequence of sustained focal AT.[239-241] In one study, tachycardia-induced cardiomyopathy was seen in 67% of patients, yet normalization of ejection fraction (EF) was common with therapy.[237] In this study, the focal atrial tachycardia mechanism was automaticity in most cases; therefore, beta-blockers are reasonable options, although in cases of treatment failure catheter ablation may be necessary. Although nonsustained focal AT may not require treatment, cardioselective beta-blockers, such as metoprolol, are known to be safe for the treatment of symptomatic pregnant patients. When tachycardia-induced cardiomyopathy is suspected, early consultation with an electrophysiologist is suggested.
6. Alternative antiarrhythmic medications are sometimes required when digoxin, beta-blockers, or calcium channel blockers are not effective in preventing recurrent SVT, including focal AT. Antiarrhythmics such as flecainide, propafenone, or sotalol are reasonable options for treatment of SVT in pregnant patients.[64] While there is limited experience using flecainide and sotalol to treat maternal arrhythmias, these medications are often used to treat fetal arrhythmias. Flecainide and propafenone are generally avoided in patients with structural or ischemic heart disease because of an increased risk of death due to arrhythmia.[242] When using antiarrhythmic drugs, FDA-mandated precautions are to be observed, with attention to using the lowest-possible effective dose.
7. Catheter ablation procedures are often avoided in pregnancy due to concerns of radiation exposure to the developing fetus; however, the risk of long-term malignancy to the fetus from the dose of radiation generally required for these procedures is negligible (see Section 4.2). Damilakis et al[163] demonstrated that the radiation exposure to the fetus during a regular electrophysiological study would not reach a threshold to cause significant risk of lifetime malignancy. When catheter ablation is deemed necessary, procedures are performed ideally after the first trimester, when feasible, with procedures using minimal or zero fluoroscopy to reduce the chances of poor fetal outcomes. Techniques for decreasing radiation exposure to mother and fetus include 3D mapping system and intracardiac echocardiogram.[243,244] Catheter ablation can be potentially curative for SVTs of diverse mechanisms, including focal atrial tachycardia.
8. Use of amiodarone in pregnancy is avoided due to its association with thyroid disorders, bradycardia, growth restriction in the fetus, and potential adverse effects in the neonate.[126] However, in pregnant patients with acute-onset or persistent SVT refractory to all other pharmacological therapies, or when other therapies, including catheter ablation, are contraindicated, intravenous or oral amiodarone remains an option. Short-term exposure to amiodarone is likely associated with fewer adverse effects on the fetus than long-term exposure.

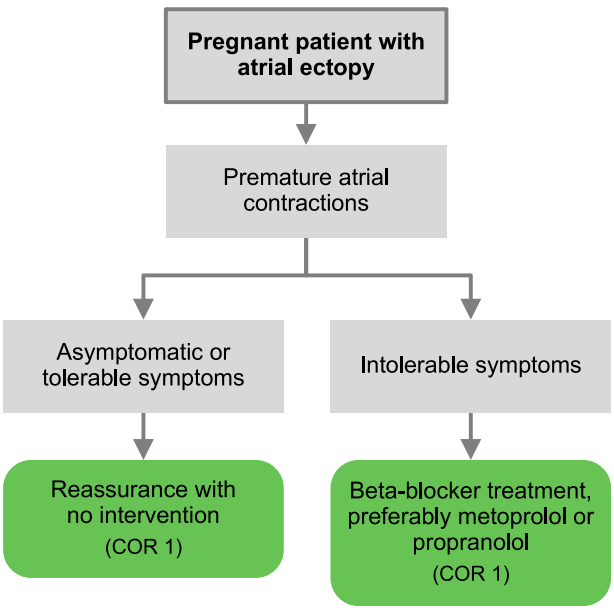

Figure 8 Algorithm of recommendations for the management of pregnant patients with atrial ectopy. Colors correspond to the class of recommendation (COR) in Table 1.

7.2. Management of atrial fibrillation and atrial flutter in pregnancy

Recommendations for the management of atrial fibrillation and atrial flutter in pregnancy			
COR	LOE	Recommendations	References
1	C-LD	1. In pregnant patients with acute-onset AF or AFL, with accompanying hemodynamic compromise or preexcitation, direct current cardioversion is recommended, with energy dosing as in the nonpregnant patient.	225,245
1	C-LD	2. In hemodynamically stable pregnant patients with AF or AFL with rapid ventricular rates (RVR), intravenous beta-blockers are recommended as the first-line option and digoxin or nondihydropyridine calcium channel blockers, alone or in combination, are recommended as second-line options for initial rate control in the absence of preexcitation.	225,226,246
1	C-LD	3. In pregnant patients with AF or AFL with persistent symptoms or RVR refractory or with contraindications to beta-blockers or calcium channel blockers, elective direct current cardioversion is recommended with anticoagulation as in nonpregnant patients.	225,245
1	C-LD	4. In pregnant patients with AF or AFL and additional risk factors that place them at high risk for thromboembolism, anticoagulation is recommended as in the nonpregnant patient.	225,226,247
2a	C-LD	5. In pregnant patients with AF or AFL with persistent symptoms or RVR refractory or with contraindications to beta-blockers or calcium channel blockers, pharmacological cardioversion with ibutilide, or flecainide in the absence of SHD, is reasonable, with the choice of drug dependent on the underlying maternal cardiac substrate.	248,249
2a	C-LD	6. In pregnant patients with AF or AFL with RVR, beta-blockers, digoxin, or nondihydropyridine calcium channel blockers alone or in combination, are reasonable for rate control with the choice of drug dependent on the underlying maternal cardiac substrate.	62,78,225,250-255
2a	C-LD	7. In pregnant patients with AF or AFL with continued symptoms or RVR despite rate control therapy, flecainide in the absence of SHD or sotalol in the absence of severe LV dysfunction are reasonable for rhythm control, with the choice of drug dependent on the underlying maternal cardiac substrate.	78,108,124,251, 252,254,256
2a	C-LD	8. In pregnant patients with hemodynamically unstable typical AFL in whom pharmacological therapy is ineffective or contraindicated, catheter ablation is reasonable with attention to and techniques for eliminating or minimizing radiation exposure to as low as reasonably achievable.	163,166
2b	C-LD	9. In pregnant patients with recurrent hemodynamically unstable AF or atypical AFL in whom pharmacological therapy is ineffective or contraindicated, catheter ablation may be considered with attention to and techniques for eliminating or minimizing radiation exposure to as low as reasonably achievable.	166
2b	C-LD	10. In pregnant patients with AF or AFL with continued severe symptoms or RVR, amiodarone may be considered when alternative pharmacological therapy and/or catheter ablation are ineffective or contraindicated.	128

Synopsis

Management of patients with AF and AFL for acute care and ongoing therapy is outlined in Figure 9. Direct current cardioversion is the first line of therapy in patients with sustained AF or AFL and hemodynamic compromise. In cases requiring ongoing pharmacological management, drug selection is based on the underlying maternal cardiac substrate, although drugs with the longest record of safe use during pregnancy are preferred. Rate control is an acceptable strategy in asymptomatic patients, but rhythm control may be necessary in the case of persistent symptoms or difficult-to-control ventricular response. The CHA_2DS_2VASc scoring system is generally calculated for evaluating thromboembolism risk with AF and AFL.[257] Catheter ablation procedures can be performed with minimal or zero fluoroscopy, with a lower threshold for performing procedures with lower complexity, such as typical AFL ablation. Amiodarone, despite its risks, remains an option in refractory cases, especially in the setting of underlying SHD.

Recommendation-specific supportive text

1. Cardioversion is generally safe during pregnancy. The majority of data show no adverse effects to the fetus with direct current cardioversion.[245] Any possible risks

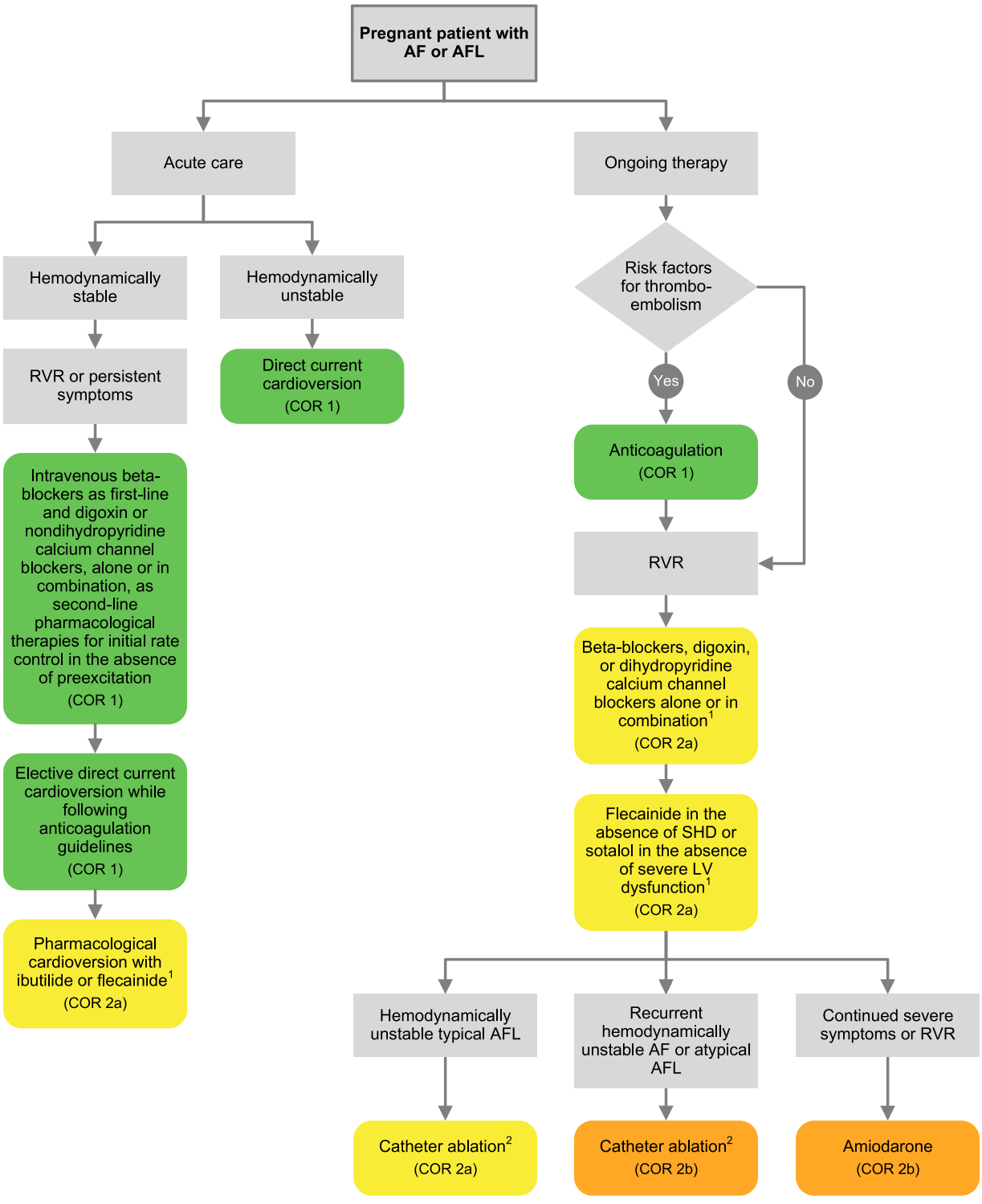

Figure 9 Algorithm of recommendations for the management of pregnant patients with atrial fibrillation (AF) and atrial flutter (AFL). Colors correspond to the class of recommendation (COR) in Table 1. [1]Choice of drug dependent on the underlying maternal cardiac substrate. [2]With attention to and techniques for minimizing radiation exposure to as low as reasonably achievable. LV = left ventricular, RVR = rapid ventricular rate, SHD = structural heart disease.

that may be imposed by shocks are generally balanced against the importance of restoring baseline maternal hemodynamics.

2. Retrospective database evaluations and case reports show relative safety and tolerance for the acute use of intravenous beta-blockers, digoxin, and/or calcium channel blockers for rate control in AF/AFL with RVR during pregnancy.[225,246]
3. Cardioversion is generally safe during pregnancy.[245] Elective cardioversion is part of a rhythm-control strategy and can be done as a standalone procedure or in combination with antiarrhythmic drug therapy. When restoring sinus rhythm, stroke prevention strategies, such as anticoagulation and transesophageal echocardiogram, should be performed as in the nonpregnant state.[5]
4. With respect to thromboembolism risk, a population-based study on the incidence of AF or AFL in the pregnant population reported an overall low CHA_2DS_2VASc score for patients without SHD, such that only 5 of 129 patients were prescribed anticoagulation with either low-molecular-weight heparins or unfractionated heparins.[225] ROPAC, however, showed that patients with SHD had a higher indication (11 of 17 patients) to receive anticoagulation.[226] In the absence of valvular heart disease, anticoagulation is generally dictated by CHA_2DS_2VASc score, as in nonpregnant patients.[9] While the thromboembolism risk is elevated during pregnancy and the immediate postpartum period, the magnitude of this risk is uncertain. Accordingly, as in the nonpregnant state, the CHA_2DS_2VASc scoring system or the presence of risk factors such as mitral stenosis are generally used to evaluate the thromboembolism risk in the case of AF and AFL.[9,257,258] Anticoagulation protocols and dosing to minimize risk of thromboembolic events should be similar to those employed for mechanical valve management in absence of AF during pregnancy, since no anticoagulation strategy specific to AF in pregnancy exists. A thorough discussion with the mother regarding the risks and benefits of the different anticoagulation approaches as they pertain to both mother and fetus is essential. Table 7 shows anticoagulation strategies in pregnancy. Of note, direct oral anticoagulants are contraindicated in pregnancy and during breastfeeding.

Table 7 Anticoagulation protocols and dosing for pregnant patients with atrial fibrillation deemed at high risk of thromboembolic events are similar to those employed for mechanical valve

Goal INR (per valve guidelines)	1st trimester	2nd trimester	3rd trimester up to 36 weeks	36 weeks to 36 hours pre-delivery	36 hours pre-delivery
Low-dose warfarin (<5 mg daily)	Continue warfarin	Continue warfarin	Continue warfarin	LMWH	UFH to stop 6 hours before delivery
High-dose warfarin (≥5 mg daily)	Continue warfarin or transition to LMWH* or UFH 6-12 weeks† with close monitoring of anti-Xa‡ or aPTT levels	Continue LMWH or change to warfarin	Continue LMWH or warfarin	LMWH	UFH to stop 6 hours before delivery

Additional information:

- Meta-analysis data in the pregnant population with mechanical heart valves show that low-dose warfarin (<5 mg daily) use throughout pregnancy has a significantly lower risk for fetal embryopathy than higher-dose warfarin (8.25% vs 0.45%, $P < 0.001$).[247]
- When higher-dose warfarin (≥5 mg daily) is needed to achieve goal INR, one may consider transitioning to heparin (UFH or LMWH) during the first trimester (6-12 weeks) vs continuation of warfarin.
- Outcomes in the population receiving UFH throughout pregnancy were overall worse for the fetus and mother; thus this strategy is not generally recommended in the valvular heart disease population unless other options do not exist (such as limited LMWH availability).[247]
- Both the *2018 ESC Guidelines for the Management of Cardiovascular Diseases During pregnancy* and the *American Heart Association Scientific Statement on the Management of Pregnancy in Patients with Complex Congenital Heart Disease* recommend frequent monitoring of peak anti-Xa levels with the transition from warfarin to LMWH, as well as the transition from LMWH back to warfarin.[12,16]
- Most data regarding DOAC use in pregnancy originates from pharmacovigilance and case report data. One review that evaluated 236 cases of DOAC exposure during pregnancy found an association between DOAC use and miscarriage, along with a 4% anomaly rate with rivaroxaban use.[267] Due to the paucity of data regarding DOAC use in pregnancy and possible safety concerns, DOAC use during pregnancy is contraindicated. Patients exposed to DOACs prior to becoming pregnant should discontinue the drug and undergo close pregnancy surveillance.[268]

*The decision regarding transitioning during this time must involve a thorough discussion with the patient as there is increased risk for embryopathy with higher-dose warfarin but a higher risk for maternal thromboembolic events with LMWH.

†LMWH preferred; UFH if LMWH unavailable

‡Plasma anti-Xa levels in pregnant women with mechanical prosthetic heart valves are generally measured 4-6 hours after the morning LMWH injection (peak levels) and with dose adjustment to achieve levels between 0.7-1.2 units/mL. anti-Xa = anti-factor Xa assay, aPTT = activated partial thromboplastin clotting time, DOAC = direct oral anticoagulants, ESC = European Society of Cardiology, INR = international normalized ratio, LMWH = low-molecular-weight heparin, UFH = unfractionated heparin.

5. A significant portion of the data regarding safety of antiarrhythmic medication use in pregnancy originates from studies related to the management of fetal arrhythmias.[78,108,251,252] In addition, both case and database reports have demonstrated ibutilide safely administered for the acute conversion of AF or AT during pregnancy without reported adverse fetal outcomes.[225,248] Intravenous magnesium is often administered prior to ibutilide to mitigate the risk of torsades de pointes (TdP).[229] Oral flecainide bolus has been shown to be effective for acute termination of AF.[259] Case reports have also shown this strategy to be effective in pregnancy, although numbers are small.[249]
6. A database report showed that up to two-thirds of women with AF or AFL and without SHD may not require continued medical therapy for AF during pregnancy.[225] In cases requiring continued maintenance, digoxin appears to be well tolerated and safe for the fetus but less effective for lowering the maternal heart rate in the setting of high adrenergic state.[78,251,252,254] While most retrospective studies have not associated beta-blocker use in pregnancy with teratogenicity, some studies have demonstrated an association of beta-blockers with low birth weight, as many of these studies cannot factor for the underlying maternal disease.[250,255] However, a study looked at a subgroup of patients without SHD who were treated with beta-blockers and found that beta-blocker use was associated with an increased risk for low birth weight.[62] With respect to the nondihydropyridine calcium channel blockers, there are reports of verapamil-associated fetal demise when used in combination with other nodal blockers, mainly in intravenous form.[73,260] More recently, a retrospective database study on the use of calcium channel blockers in more than 800 women during pregnancy did not find a significantly increased risk for congenital anomalies.[253]
7. The majority of the data regarding the safety of flecainide has been obtained in the fetal SVT population but is applicable to other maternal arrhythmias, in view of the record of safety. Most of the studies have shown fairly good maternal and fetal tolerance to flecainide. In cases of maternal AFL, flecainide may increase conduction in the AV node and should be used with caution. Propafenone use during pregnancy has also been reported and is generally well tolerated, although the data are more limited compared with flecainide.[78,108,251,252] Similar to flecainide, most data regarding the safety profile of sotalol during pregnancy have been collected in the setting of treatment for fetal SVT, and sotalol likewise appears to be well tolerated by the fetus, particularly when used at a dose of less than 320 mg per day, with standard monitoring recommended for the mother. In absence of concomitant fetal hydrops, sotalol appears to be well tolerated when initiated between the second and third trimesters.[124,254,256]
8. Recent guidelines for the management of adult patients with SVT recommend catheter ablation as a class I option for rhythm management of AFL.[8,19] Additionally, there is increasing operator experience with minimal to no fluoroscopy ablation, particularly for arrhythmias that are right atrial in origin.[261,262] Owing to the highly successful nature of right-sided typical AFL ablation, catheter ablation is a reasonable option, after careful evaluation of the risks and benefits in the pregnant patient, and ideally should be performed in a center or by operators experienced in ablation techniques that eliminate or minimize fluoroscopy exposure.[19,164,243,263,264]
9. In select cases in which persistent AF or atypical AFL present a risk to the mother or fetus, and there is a contraindication to or failure of pharmacological therapy, catheter ablation utilizing minimal to no fluoroscopy remains an important option. An important consideration is the complexity of the procedure, as the risk of potential complications is higher and the ability to minimize fluoroscopy use may be less predictable. Ideally, the procedures should be performed in a center or by operators experienced in ablation techniques that eliminate or minimize fluoroscopy exposure.[164,166,243,262,265]
10. Amiodarone remains an option for treatment of refractory arrhythmias when the potential benefit warrants its use, despite potential risks, after a careful assessment of the risks and benefits and keeping in mind the duration of use, severity of the arrhythmia, fetal gestational age and underlying maternal substrate. Amiodarone therapy is indicated for the shortest duration possible. The most common fetal complication is fetal hypothyroidism, which is typically transient and treated effectively with short-term maternal therapy.[128] Therefore, fetal monitoring for signs of clinical hypothyroidism is necessary; it is also important to monitor and treat maternal thyroid indices in the setting of clinical thyroid dysfunction.[266] In addition, amiodarone has the potential for direct neurotoxicity, which may lead to neurodevelopmental abnormalities.[126] With respect to other antiarrhythmic medications, very limited data exist for the use of dofetilide during pregnancy; nevertheless it can be used with consideration of the risks versus benefits.

7.3. Management of ventricular arrhythmias in pregnancy not associated with inherited arrhythmia syndromes

Recommendations for the management of ventricular arrhythmias in the pregnancy not associated with inherited arrhythmia syndromes			
COR	LOE	Recommendations	References
1	C-LD	1. In pregnant patients with sustained VT and hemodynamic compromise, direct current cardioversion is recommended, with energy dosing as in the nonpregnant patient.	245,269,270
1	C-LD	2. In pregnant patients with idiopathic VT and hemodynamic stability, intravenous beta-blocker or adenosine for outflow tract VT and intravenous verapamil for fascicular VT are recommended as first-line options.	271-275
1	C-LD	3. In pregnant patients with hemodynamically stable VT, when pharmacological therapy is deemed necessary, intravenous procainamide is recommended for acute therapy.	229,276-278
1	C-LD	4. In pregnant patients with sustained VT refractory or with contraindications to beta-blockers and/or other antiarrhythmic drugs, synchronized cardioversion is recommended, with energy dosing as in the nonpregnant patient.	245,269,270
1	C-LD	5. In pregnant patients who meet indications for implantable cardioverter defibrillator (ICD) placement due to sustained ventricular arrhythmias or due to high risk for sudden cardiac death, device implantation is recommended with attention to and techniques for eliminating or minimizing radiation exposure to as low as reasonably achievable.	269,279-282
1	C-LD	6. In pregnant patients with ICDs prior to pregnancy, it is recommended to continue routine ICD care according to the underlying cardiac substrate.	269,279,283,284
1	C-LD	7. In women who are considering pregnancy and would otherwise meet indications for ICD, pacemaker, or cardiac resynchronization therapy device placement, these procedures should be performed prior to pregnancy and according to the underlying cardiac substrate.	280-282
1	C-LD	8. In pregnant patients with chronic or recurrent VT, beta-blockers, alone or in combination with other antiarrhythmic drugs, are recommended for arrhythmia suppression due to their overall safety profile in pregnancy.	62,255,285
1	C-LD	9. In pregnant patients with recurrent VT refractory or with contraindications to beta-blockers who require additional antiarrhythmic drug therapy, treatment with flecainide, sotalol, or mexiletine is recommended with the choice of drug based on the underlying cardiac substrate.	78,108,124,251,252,254,256,286
2a	C-LD	10. In pregnant patients with recurrent symptomatic or hemodynamically unstable VT in whom pharmacological therapy is either ineffective or contraindicated, catheter ablation is reasonable with an experienced operator and with attention to and techniques for eliminating or minimizing radiation exposure to as low as reasonably achievable.	166,287,288
2a	C-LD	11. In pregnant patients with recurrent VT associated with hemodynamic impairment or ICD shocks, amiodarone is reasonable for arrhythmia suppression if alternative therapies, including ablation, are contraindicated or ineffective.	128,285
2b	C-LD	12. In pregnant patients who meet indications for sudden death prevention due to high-risk features or VT that may be of a reversible etiology, such as peripartum cardiomyopathy, a wearable cardioverter defibrillator may be reasonable.	289,290

Synopsis

For hemodynamically significant VT, direct current cardioversion has been shown to be safe during pregnancy. When pharmacological therapy is deemed necessary, the choice of antiarrhythmic agent depends on the etiology of the specific ventricular arrhythmia and underlying cardiovascular substrate. It is ideal if patients considering pregnancy undergo ablation therapy or ICD placement before conception; however, the procedure can be performed safely during pregnancy when needed. When

drug therapy is required, drugs with the longest record of safe use during pregnancy, such as sotalol or intracordal agents, are preferred in the absence of SHD. Catheter ablation can be done safely in pregnancy, especially when performed with minimal or no fluoroscopy use. Amiodarone remains an option for refractory cases, or when alternative options are contraindicated. An algorithm of the recommendations for the management of pregnant patients with ventricular arrhythmias is shown in Figure 10.

Recommendation-specific supportive text

1. Direct current cardioversion is generally safe during pregnancy and effective particularly in cases of hemodynamic compromise. The majority of data show no adverse effects to the fetus with direct current cardioversion.[245,270,291] Furthermore, literature in the ICD population also supports the lack of significant risk to the fetus with maternal ICD shocks.[269] Any possible risk to the fetus that may be imposed by shocks must be balanced against the importance of restoring baseline maternal hemodynamics.
2. Data show that outflow tract ventricular arrhythmias in pregnant patients with structurally normal hearts tend to respond well to beta-blockers.[273,275] Additionally, adenosine appears to be well tolerated by both mother and fetus during pregnancy and may also be used to treat outflow tract VT.[271,292] Importantly, repletion of potassium and/or magnesium may be required for patients who are at risk for significant electrolyte disturbances presenting with outflow tract arrhythmias. One case report described such a situation in which outflow tract VT was successfully treated with magnesium repletion in a patient with severe hypomagnesemia and hypokalemia due to hyperemesis gravidarum.[293] For the acute management of fascicular VT, intravenous verapamil has been used successfully without maternal or fetal complications.[272,274]
3. In the general population, data show that procainamide is better tolerated and more effective than amiodarone for acute termination of monomorphic VT.[278] Similarly, procainamide efficacy was higher than lidocaine when evaluated in both small randomized prospective and retrospective studies.[276,277] With respect to safety in pregnancy, a case report detailed procainamide use for successful management of sustained VT in a pregnant patient without any adverse fetal or maternal effects.[229] There are no data on intravenous sotalol use in pregnancy.
4. Cardioversion is generally safe in pregnancy.[245,269,270,291] Any possible risk that may be imposed by shocks must be balanced against the importance of restoring baseline maternal hemodynamics.
5. As with pacemakers, transvenous ICD placement can be performed safely during pregnancy when deemed appropriate with the utilization of strategies for minimizing fluoroscopy exposure, including use of single-lead or subcutaneous systems where possible (refer to Section 4.2 for radiation-reduction strategies). In general, the fluoroscopy requirements of transvenous ICD placement are low enough that the benefits to the mother outweigh the risks of radiation. While there does not appear to be harm when performing defibrillation testing, the necessity of such testing should be weighed against possible risk of arrhythmia-induced hypotension.[279] While a subcutaneous ICD would negate the risk of fluoroscopy, and a single case report has described delivery management in the event of a previously placed subcutaneous ICD, data are lacking regarding implantation of subcutaneous ICDs during pregnancy.[294]
6. Most reports have not shown an increase in ICD-related complications during pregnancy compared with the general ICD population, particularly for prepectoral transvenous systems.[269,279,283,284] Measures, such as the use of beta-blockers or antiarrhythmic drugs, for avoiding sustained hemodynamically unstable arrhythmias may be considered in high-risk patients after weighing the risks and benefits of such approaches.[283,284] Notably, appropriate ICD therapies, such as shocks, do not appear to have detrimental effects on the fetus.[269,279,283,284]
7. Device placement has been performed safely during pregnancy, with measures to avoid fetal fluoroscopy exposure; however, there is less risk to the fetus if devices are implanted prior to pregnancy.[280-282] Since arrhythmias tend to worsen during pregnancy, pregnancy in women with indications for cardiovascular implantable electronic devices can carry some additional risks. In these cases, preconception counseling regarding maternal and fetal risk from the underlying disease is crucial. Device implantation prior to pregnancy in these cases can reduce both the risk of arrhythmic complications during pregnancy and risks to the fetus if the procedure became necessary during pregnancy.

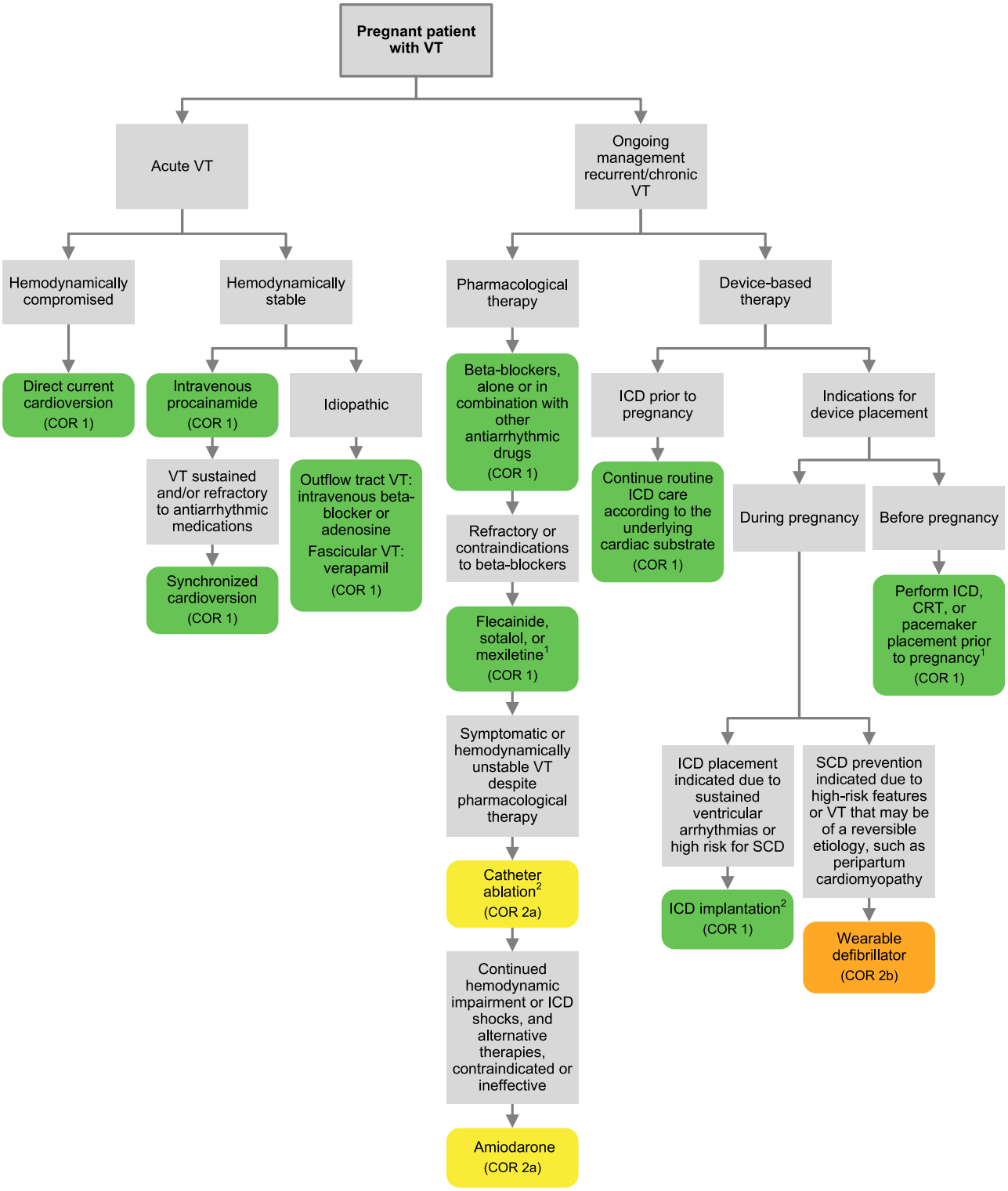

Figure 10 Algorithm of recommendations for the management of pregnant patients with ventricular arrhythmias. Colors correspond to the class of recommendation (COR) in Table 1. [1]Choice of drug dependent on the underlying cardiac substrate. [2]With techniques for minimizing fluoroscopy as low as reasonably achievable. CRT = cardiac resynchronization therapy, ICD = implantable cardioverter-defibrillator, SCD = sudden cardiac death, VT = ventricular tachycardia.

8. Registry data show that most pregnant women with SHD and VT treated with medications receive beta-blockers.[285] Importantly, beta-blocker use has not been associated with teratogenicity, although some beta-blockers have been associated with low fetal birth weight. Therefore, prospective benefits for arrhythmia suppression must be thoroughly evaluated against that potential risk.[62,255]
9. Most safety data regarding the use of sotalol and flecainide during pregnancy are derived from the management of supraventricular fetal arrhythmias during pregnancy, and the most commonly studied class IC agent has been flecainide over propafenone.[15] While propafenone appears to be safe and is used, data on its use are scant compared with that on flecainide. In general, flecainide and sotalol are well tolerated by both the fetus and the mother. For sotalol, the dose is less than 320 mg per day administered under standard cardiac monitoring. In the absence of concomitant fetal hydrops, sotalol appears to be well tolerated when initiated between the second and third trimesters.[78,108,124,251,252,254,256] However, caution is advised when using sotalol in pregnant patients with significant ventricular dysfunction. Case report data show that mexiletine may be safe for both the pregnant patient and the fetus.[286]
10. Hemodynamically significant VT can be potentially life threatening to both the mother and fetus. Ablation during pregnancy for medically refractory VT has been reported. Sadek et al[166] described a fluoroscopy-free ablation in a pregnant patient with refractory VT in the setting of ACM, whereas Lahiri et al[288] described a fluoroscopy-free ablation for medically refractory fascicular VT in a pregnant patient. Kambiré et al[287] reported on a patient with persistent outflow tract VT refractory to medical therapy necessitating ablation. All cases were notable for the lack of complications.
11. The ROPAC database reported the use of amiodarone in 7.1% of cases of VT in the setting of maternal heart disease.[285] The most common fetal complication is fetal hypothyroidism, which is typically transient and effectively treated with short-term therapy.[128] Therefore, fetal monitoring for signs of clinical hypothyroidism is necessary. In addition, amiodarone has the potential for direct neurotoxicity, which may lead to neurodevelopmental abnormalities.[295] Nevertheless, the potential risk has to be balanced against the detrimental effects of intractable ventricular arrhythmia to both the mother and fetus. Dose and duration of amiodarone therapy should be minimized as much as possible.
12. Peripartum cardiomyopathy can be associated with ventricular arrhythmias.[270] However, the prospective Investigations of Pregnancy Associated Cardiomyopathy study showed that 72% of patients with peripartum cardiomyopathy experienced recovery (EF >50%) by 1 year postpartum, thus negating the need for permanent sudden cardiac death prevention with an ICD.[296] As such, an alternative to ICD placement during pregnancy is a wearable cardioverter defibrillator, particularly if the cardiomyopathy was expected to recover. However, predictors of those who would most benefit from this therapy are not well established. Notably, a database report of wearable cardioverter defibrillator use in 107 patients with peripartum cardiomyopathy showed no appropriate or inappropriate shocks in the population; 12 of the patients were prescribed the wearable cardioverter defibrillator prepartum.[289] Conversely, Duncker et al[290] showed that 3 of 7 patients with peripartum cardiomyopathy (mean EF = 18%) received 4 appropriate and successful wearable cardioverter defibrillator shocks for VF, such that the authors of that study recommended consideration of the wearable cardioverter defibrillator in patients with peripartum cardiomyopathy and severely reduced EFs. Furthermore, the Investigations of Pregnancy Associated Cardiomyopathy study also showed that patients with peripartum cardiomyopathy and an EF ≤30% with an LV end diastolic diameter ≥6.0 cm did not recover by 1 year postpartum.[296] As such, patients with a large LV end-diastolic diameter coupled with a severely reduced EF may warrant ICD implantation earlier in the process.

Section 8 Management of pregnant patients with bradycardia and/or heart block

Bradycardia is an unusual finding in pregnancy. Pregnant patients with bradycardia should undergo evaluation similar to that indicated in the nonpregnant population, including a detailed history and physical examination.[11] Complete AV block in the absence of SHD is generally well tolerated in pregnancy.[297] Establishing an association between bradycardia and symptoms is the key to determining whether a pacemaker is indicated.[298] When pacemaker implantation is deemed necessary during pregnancy, strategies can be used to minimize fluoroscopy exposure, including application of current technologies and single-lead systems (see Section 4.2 for radiation-reduction strategies).[299] Temporary ventricular pacing remains a temporizing option that can be individualized as indicated.

Recommendations for management of pregnant patients with bradycardia and/or heart block			
COR	LOE	Recommendations	References
1	C-LD	1. In pregnant patients who present with advanced heart block or conduction system disease, evaluation with transthoracic echocardiogram is recommended with cardiac MRI reserved for select cases when myocardial and/or infiltrative processes are suspected and if done in the postpartum period.	300,301
1	C-LD	2. In pregnant patients with irreversible symptomatic bradycardia due to third-degree or second-degree Mobitz type II heart block or severe sinus node dysfunction, with syncope or presyncope that may place the mother and/or the fetus at risk, permanent pacemaker placement is recommended, with attention to and techniques for eliminating or minimizing radiation exposure to as low as reasonably achievable.	280-282,299
1	C-LD	3. In pregnant patients with symptomatic bradycardia refractory or with contraindications to pharmacological therapy, temporary ventricular pacing is recommended for those at risk of hemodynamic instability and/or syncope in the peripartum period.	302-304
1	C-LD	4. In pregnant and postpartum patients with asymptomatic sinus bradycardia or Mobitz type I AV block without evidence of SHD, reassurance is recommended with no need for intervention.	305
2a	B-NR	5. In pregnant patients with hemodynamically stable and asymptomatic congenital heart block who were deemed potential candidates for permanent pacemaker placement prior to pregnancy, it is reasonable to defer the decision on device implantation until after delivery.	303,304,306
3: No benefit	B-NR	6. In pregnant patients with hemodynamically stable and asymptomatic congenital heart block with an acceptable ventricular rate, a narrow QRS complex, and normal ventricular function, prophylactic temporary pacemaker placement around the time of delivery is not recommended.	297,306,307

Synopsis

Cardiac pacemakers appear to be well tolerated during pregnancy.[269,279,283,284,303,306] The frequency of monitoring and follow-up should center around the underlying maternal disease. When cardiac device implantation is indicated during pregnancy, device placement should be performed with care to minimize fluoroscopy exposure to the fetus.[280-282] Conversely, when there is no strong indication for device placement, particularly in cases of stable congenital AV block, pregnancy does not appear to increase the risk from this etiology of AV block. As such, temporary pacing during pregnancy or delivery is not usually necessary.[306] Recommendations for the management of pregnant patients with bradycardia and/or heart block are summarized in Figure 11.

Recommendation-specific supportive text

1. Although in a majority of pregnant patients who present with advanced heart block the etiology is congenital, other diagnostic possibilities must be excluded. Transthoracic echocardiography can reveal conditions such as cardiomyopathy, valvular disease, congenital defects, tumors, infiltrative processes, and pericardial and great vessel abnormalities.[29,308] Cardiac MRI is particularly useful if additional information is required to identify infiltrative disease processes in select cases, or when echocardiography is not feasible or of poor quality, especially when those diagnostic possibilities are suspected based on the clinical presentation.[219] However, the use of gadolinium is typically avoided during pregnancy, in view of concerns for potential of causing harm to the fetus based on theoretical considerations and animal studies.[309] Thus, gadolinium studies are best done in the postpartum period, except in cases where the benefits clearly outweigh the possible risks to the fetus, which are for the most part unknown.
2. Minimizing fluoroscopic exposure to the fetus is discussed in Section 4.2. In the case of pacemaker implantation, modern technology enables placement of the pacemaker with no fluoroscopy or with minimal exposure.[280-282] Vascular access may be obtained utilizing landmark or ultrasound guidance.[281,282] Evaluation of lead position may be obtained via intracardiac echocardiography; even when fluoroscopy is required, radiation can be kept to low amounts, in some cases even as low as <1 second.[282]
3. The use of temporary transvenous pacemakers has been reported in pregnant women with symptomatic bradycardia around the time of delivery.[310] Dalvi et al[302] reported 3 cases that required temporary pacing during labor; however, only 2 required permanent pacemaker after delivery due to recurrence of symptoms with weaning of temporary pacing.[302] Although data are limited, temporary pacing may be used as a bridge to permanent pace-

maker placement either before or after delivery, depending on the clinical circumstances, in a patient with hemodynamically significant bradycardia, especially if pharmacological options such as isoproterenol are ineffective or contraindicated.[302,303]

4. Sinus bradycardia is rare during pregnancy since the physiological response is for the pulse to accelerate 10-20 bpm over baseline to increase cardiac output. Yet, modest bradycardia can be seen after delivery.[311] Mobitz type I AV block is common and rarely implies progressive conduction system disease.[11] Both situations can be benign in the absence of hemodynamic impairment and SHD.[305]
5. Hidaka et al[306] reported their experience with 32 pregnancies in the setting of high-grade AV block without pacemaker. Of note, a significant portion of these patients had congenital heart block, and therefore had relatively stable junctional escape rhythms. While all patients did well during pregnancy, 1 patient suffered from syncope and sudden death 1 month postpartum; thus, close surveillance of pregnant patients with complete AV block is warranted, and implantation of pacemakers during or after pregnancy should follow guideline-based recommendations for the general population.[306] Data also show that patients with baseline AV nodal block may experience worsening AV nodal function during pregnancy, with function usually improving to baseline postpartum.[303,306]
6. Delivery appears to be well tolerated in hemodynamically stable pregnant patients with advanced AV block who are asymptomatic with an acceptable ventricular rate, a narrow QRS complex, and normal ventricular function. Reported cases in the literature support conservative management, especially in the setting of congenital heart block patients with narrow escape rhythms. Pacemaker implantation is not indicated in these patients around the time of delivery.[306]

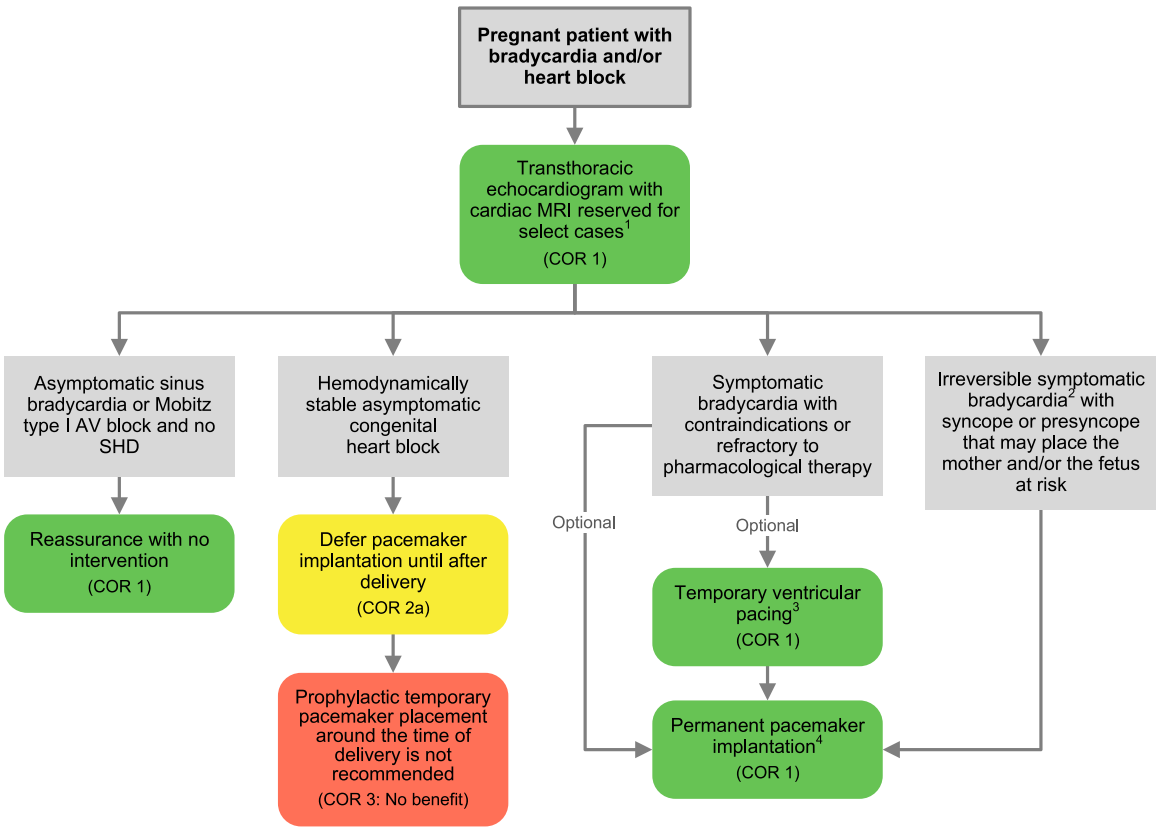

Figure 11 Management of bradycardia and/or heart block in the pregnant patient. Colors correspond to the class of recommendation (COR) in Table 1. [1]Cardiac magnetic resonance imaging (MRI) should be reserved for select cases in which myocardial and/or infiltrative processes are suspected and if done in the postpartum period. [2]Due to third-degree or second-degree Mobitz type II heart block or severe sinus node dysfunction. [3]For patients at risk of hemodynamic instability and/or syncope in the peripartum period. [4]With attention to and techniques for eliminating or minimizing radiation exposure to as low as reasonably achievable. AV = atrioventricular, SHD = structural heart disease.

Section 9 Advanced cardiac life support for the pregnant patient

Advanced cardiac life support (ACLS) recommendations are provided here because of their frequent association with arrhythmias during pregnancy; however, many of these recommendations also apply to nonarrhythmic cardiac arrests during pregnancy. Additional guidance can be found in the *AHA Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care*.[312]

Recommendations for advanced cardiovascular life support for the pregnant patient

COR	LOE	Recommendations	References
1	B-NR	1. Obstetric caregivers should monitor high-risk pregnant patients for early warning signs of impending cardiovascular instability in order to activate cardiovascular life support teams in a timely manner.	313
1	C-LD	2. Basic life support (BLS) and ACLS response in obstetric centers should include plans for immediate activation of a specialized obstetric-oriented code team with preparation for resuscitative hysterotomy and simultaneous activation of a neonatal code team.	314-316
1	C-LD	3. In the pregnant patient with cardiac arrest in the earlier parts of gestation, cardiopulmonary resuscitation (CPR) should be performed as in nonpregnant patients.	317
1	C-LD	4. In the pregnant patient undergoing CPR in the latter part of gestation when the uterine fundus is above the level of the maternal umbilicus, leftward and upward displacement of the uterus should be performed.	174,175,318
1	C-LD	5. Chest compressions of the pregnant patient should be done with the hands placed in the center of the lower half of the sternum as in the nonpregnant patient.	319
1	C-LD	6. In pregnant patients with a shockable rhythm, immediate defibrillation and medical management of arrhythmia should be provided as in nonpregnant patients, including standard defibrillation energy dose recommendations.	161
1	C-LD	7. In pregnant patients, defibrillator pad placement should be in the anterolateral position as in nonpregnant patients, but the lateral pad should be placed below and/or lateral to avoid breast tissue.	155,160,161
1	C-LD	8. In pregnant patients with in-hospital cardiac arrest when uterine evacuation is deemed necessary, resuscitative hysterotomy should be performed at the site of the arrest.	317,320,321
1	C-EO	9. In pregnant patients with cardiac arrest, resuscitation efforts and defibrillation of a shockable rhythm should be administered immediately, without delays for fetal assessment/monitoring or the removal of fetal monitoring devices.	
1	C-EO	10. In pregnant patients undergoing CPR, ACLS medication should be given as in the nonpregnant patient without concern for fetal exposure or teratogenicity.	
2a	C-LD	11. In pregnant patients with cardiac arrest at >20 weeks' gestational age or if uterine fundus is palpable above the umbilicus, it is reasonable to perform resuscitative hysterotomy early in resuscitative efforts, with the goal of uterine evacuation ideally within 5 minutes of the onset of cardiac arrest, to maximize the chance of maternal survival.	317,322,323
2a	C-LD	12. In pregnant patients with cardiac arrest, resuscitative uterine evacuation with assisted vaginal delivery is reasonable as an alternative to resuscitative hysterotomy, if deemed feasible by the obstetric team.	324

Synopsis

Except for some isolated differences, in general, the management of cardiac arrest in the pregnant patient is the same as in nonpregnant patients, although a multidisciplinary approach, including coordination among maternal, obstetric, and neonatal resuscitation teams, is critical to optimizing maternal and neonatal outcomes. Cardiac arrest is a rare obstetric complication that poses a great challenge to obstetric caregivers because of the need for simultaneous implementation of BLS and/or ACLS and preparation for resuscitative uterine evacuation. A summary of the recommendations for management of the pregnant patient with ACLS is provided in Figure 12.

Recommendation-specific supportive text

1. Recognition of women at risk of clinical deterioration allows for initiation of monitoring and the opportunity for cardiovascular stabilization, resulting in significant reductions in maternal morbidity. The clinical criteria to be monitored include maternal heart rate >130/min, respiratory rate >30/min, mean arterial pressure <55

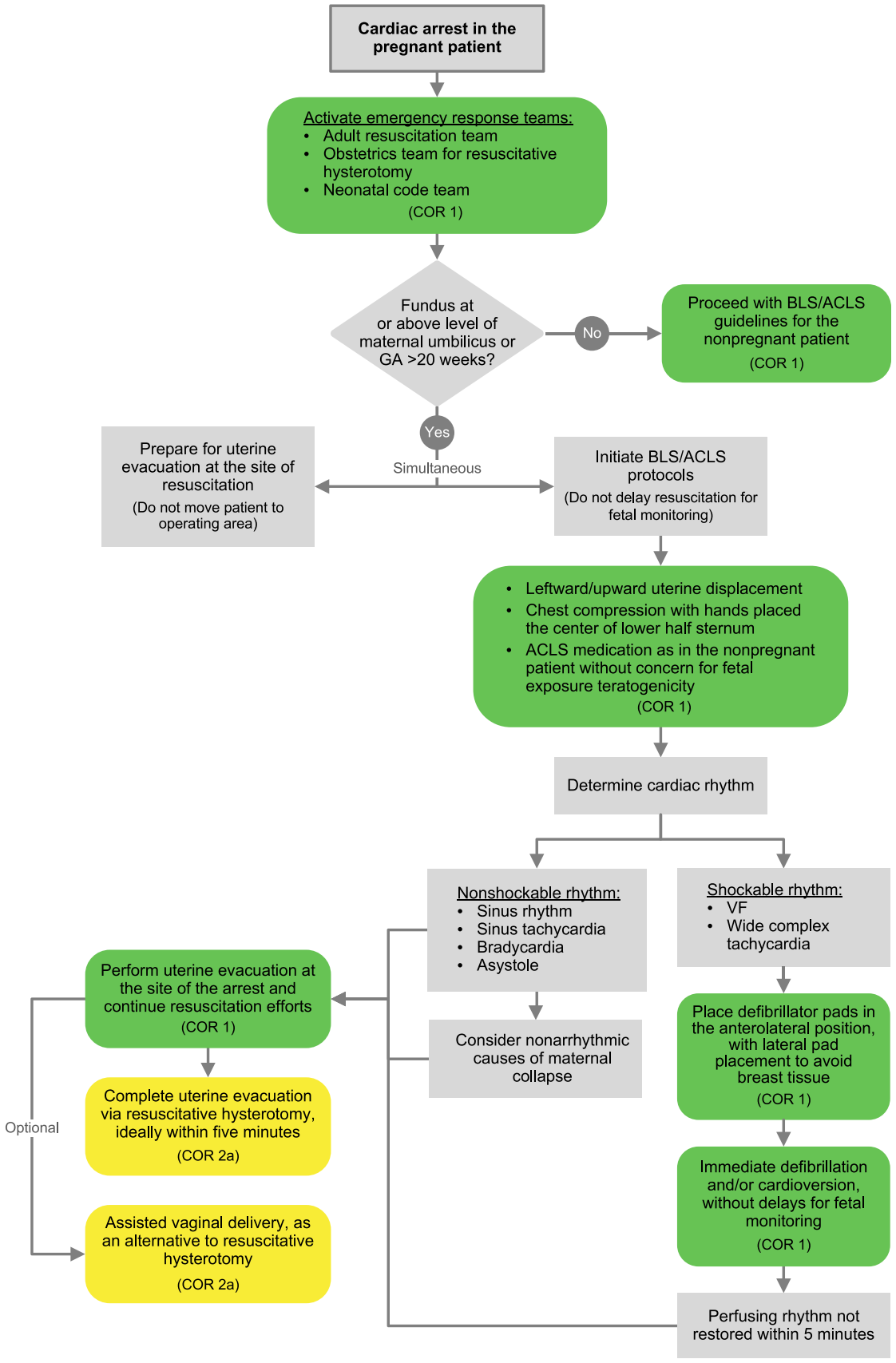

Figure 12 Management of cardiac arrest in the pregnant patient. Colors correspond to the class of recommendation (COR) in Table 1. ACLS = advanced cardiac life support, BLS = basic life support, GA = gestational age, VF = ventricular fibrillation.

mmHg, oxygen saturation <90%, abnormal body temperature, fetal heart rate >160/min, altered mental status, and pain out of proportion to stage of labor.[313]

2. Coordination of multidisciplinary emergency response teams is challenging and can result in delays in delivery of lifesaving care, particularly in the obstetric setting. Organization of specialized combined obstetric and neonatal emergency response teams has been shown to improve team performance in simulation-based training. Mobilization of multidisciplinary teams must be immediate and simultaneous, with caregivers initiating BLS, ACLS, and preparation for uterine evacuation simultaneously.[314-316]
3. Management of cardiac arrest during pregnancy is the same as for nonpregnant adult patients, especially in earlier stages of pregnancy, when a smaller uterus does not cause aortocaval compression and as such would not compromise blood return.[22,23]
4. At approximately 20 weeks, the uterine fundus is palpable at the level of the umbilicus and may start to adversely affect hemodynamics in the supine pregnant woman via aortocaval compression. Decompression of these major vessels by manual leftward and upward displacement of the uterus (Figure 13) by a first responder may significantly improve hemodynamics during resuscitation, without interfering with resuscitative efforts, including chest compressions.[21,174,175] Alternatively, Butcher et al,[318] using a manikin model, compared the effectiveness of chest compressions in the supine position with manual uterine displacement versus lateral tilt with a foam-rubber wedge, and concluded that either method was suitable for CPR in pregnant women, although a number of participants in the study found it easier to provide CPR with manual displacement. Additional benefits of manual left uterine displacement over tilt may include easier airway management and defibrillation, since the patient remains supine.

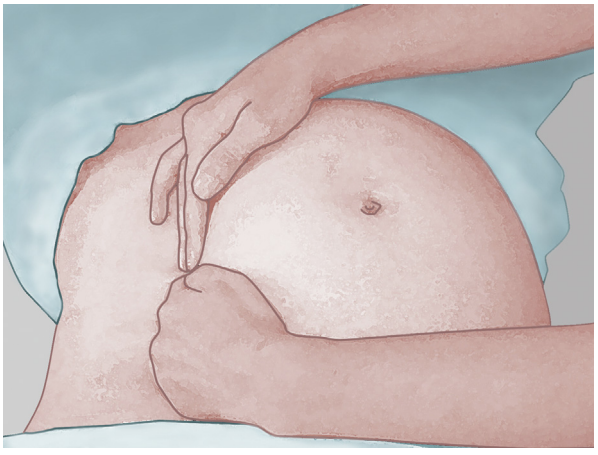

Figure 13 Manual leftward and upward uterine displacement.

5. There is no evidence of cardiac displacement by the effect of the gravid uterus, even in a full-term pregnancy. Modification of hand position for chest compressions is therefore not necessary for the resuscitation of the pregnant patient.[22,319] As in nonpregnant patients, it is important to prioritize the efficacy of chest compressions during resuscitation, and chest compression quality is maximized when the pregnant patient is flat on a firm surface.[318,325]
6. Immediate defibrillation of a shockable rhythm is associated with improved survival. Thoracic impedance, which is an important determinant of defibrillation efficacy, is not significantly altered in pregnancy, and therefore standard energy doses are administered as in nonpregnant patients.[22,23,161]
7. Thoracic impedance, when measured through defibrillation pads placed in the standard anterolateral position, is adversely affected when the lateral defibrillation pad is placed on the breast, when compared with placement below breast tissue on the chest wall (see Section 4.1).[160]
8. Transportation of the patient from the site of cardiac arrest for resuscitative hysterotomy is associated with significant delay in completion of the procedure, and with worse maternal and neonatal outcomes. For this reason, it is crucial to prepare for and complete uterine evacuation wherever resuscitation is being performed (an operating room is not required).[317,320,321]
9. Identification of a shockable rhythm and immediate cardioversion or defibrillation are critical to maternal and fetal survival of cardiac arrest. Maternal defibrillation or cardioversion is unlikely to have adverse effects on fetal cardiac rhythm, or on fetal monitoring systems placed externally or internally (fetal scalp monitor). For this reason, it is critical that maternal defibrillation is not delayed for the initiation or discontinuation of fetal monitoring procedures. Additionally, fetal monitoring could interrupt or distract caregivers from maternal resuscitation efforts.
10. Although pregnancy can alter the pharmacokinetics of cardiovascular medications with respect to clearance and metabolism, as well as volume of distribution, there is insufficient evidence to warrant different pharmacological management of arrhythmias during resuscitation of pregnant patients from that indicated for nonpregnant patients.[60,326,327] The ideal location for intravenous access is above the diaphragm. If it is not possible to place the IV centrally, the interosseus humerus is a good alternative location.
11. During cardiac arrest, the most immediate goal is restoring maternal hemodynamics. Uterine evacuation during maternal resuscitation has been shown to improve maternal and neonatal survival, particularly if completed very early after the onset of cardiac arrest. In fact, some case reports have demonstrated return of spontaneous circulation only after the uterus was evacuated.[328] The goal is to initiate delivery within 5 minutes to minimize risk of hypoxic brain injury to the fetus. In a study of cardiac arrest in the United Kingdom, perimortem cesarean delivery was performed in 49 women; the time from collapse to perimortem cesarean section was significantly shorter in women who survived (median interval 3 vs 12 minutes, $P = 0.001$).[317] However, the goal to initiate delivery within 5 minutes is rarely achieved,

and successful outcomes of evacuation have been reported after much longer intervals since the onset of the arrest.[21] Preparation for resuscitative hysterotomy (or perimortem cesarean delivery) is therefore a key part of initial maternal resuscitative efforts to maximize maternal and neonatal survival.[317,322,323,328,329]

12. If maternal cardiac arrest occurs during labor, provided that the cervix is fully dilated, assisted vaginal delivery may be an alternative to resuscitative hysterotomy to evacuate the uterus. In 1 small series that included 5 pregnant patients with cardiac arrest, 2 underwent vaginal deliveries that resulted in good maternal and fetal outcomes regardless of the time between the arrest and delivery. The authors suggested as a possible explanation that the patients were either fully dilated or pushing at the time of arrest, allowing prompt delivery.[324]

Section 10 Arrhythmia management in the pregnant patient with arrhythmogenic structural cardiac substrates

Patients with preexisting arrhythmogenic cardiac conditions (SHD, CHD, valvular heart disease, ACM, and hypertrophic cardiomyopathy [HCM]) are particularly at risk for arrhythmias during pregnancy. The arrhythmias associated with these conditions are likely more common during pregnancy due to physiological stress, including associated hormonal changes and increased volume. In turn, a first manifestation of arrhythmias during pregnancy may indicate the presence of an undiagnosed underlying cardiac condition. Thus, comprehensive evaluation of a patient with no prior cardiac disease presenting with new arrhythmias should include evaluation for structural abnormalities. This is important because the selection of therapies can be dependent on the underlying condition.

10.1. Arrhythmia management in the pregnant patient with structural heart disease

Recommendations for arrhythmia management of the pregnant patient with structural heart disease

COR	LOE	Recommendations	References
1	C-LD	**1. Patients with SHD and a history of arrhythmias who are contemplating pregnancy should have preconception counseling.**	46,330-332
1	C-LD	**2. Pregnant patients who present with new complex SVT or VT should undergo an evaluation for SHD.**	46,330-333
1	C-LD	**3. Pregnant patients with preexisting SHD who develop new arrhythmias during pregnancy should have a clinical and echocardiographic evaluation to exclude changes in cardiac structure and/or function.**	46,330-332

Synopsis

SHD may coexist with incident arrhythmias during pregnancy. Given the physiological stress of pregnancy, previously undiagnosed structural abnormalities may manifest for the first time during the pregnancy period. Thus, when a patient presents with new arrhythmias, it is important to evaluate clinically and echocardiographically for new or worsening structural cardiac abnormalities. Furthermore, some medications used to manage patients with SHD may be contraindicated during pregnancy. Thus, preconception counseling is valuable to advise on risk during pregnancy to the mother and the fetus, and to consider appropriate medications.

Recommendation-specific supportive text

1. Patients with preexisting SHD may be at higher risk of maternal and fetal complications than individuals without heart disease. Roos-Hesselink et al[332] demonstrated that, among 1321 women with CHD, valvular heart disease, ischemic heart disease, and cardiomyopathy, maternal death occurred in 1% of the population, compared with 0.007% in an otherwise normal population. Similarly, fetal and neonatal mortality were higher than in the normal population. Of note, both maternal and fetal/neonatal mortality were higher in developing countries. Drenthen et al[334] reported that the most common pregnancy-related complications include arrhythmias and heart failure. Thus, given the high incidence of events, it is important to have clear discussions regarding the risks and likelihood of successful pregnancy, with preconception counseling provided by a cardiologist or electrophysiologist and maternal-fetal medicine specialist with expertise in the management of pregnant patients with cardiovascular disease.
2. In general, new arrhythmias, such as atrial or ventricular arrhythmias, that occur during pregnancy are uncommon. However, when they do occur, they can indicate

the presence of preexisting or previously unrecognized SHD.[15] This is relevant in nonpregnant and pregnant patients, with echocardiography and clinical evaluation being critical to rule out SHD. Recognition of the presence of underlying heart disease may, in turn, help inform the patient regarding risk of maternal or fetal events.[330,332,334] In addition to clinical evaluation and echocardiography, an ECG is also important when the patient is in sinus rhythm, as the presence or absence of ECG abnormalities (eg, conduction system disease) may suggest the presence of disease requiring more advanced imaging (eg, MRI).

3. It is well recognized that pregnancy can be associated with increased physiological stress on the heart. Thus, in patients with known SHD, there is the potential for further decompensation depending on the specific cardiac lesion. This may manifest as incident arrhythmias during pregnancy. Thus, in patients with known SHD, it is important to ensure that there has not been deterioration in cardiac function or structure. Silversides et al[46] and Drenthen et al[334] demonstrated that while arrhythmias were the most common cardiac complication in patients with SHD, heart failure was second most common. The development of new arrhythmias may portend worsening cardiac status.

10.2. Arrhythmia management in the pregnant patient with congenital heart disease

Since the 1960s, surgical intervention for CHD, coupled with advances in medical and cardiac implantable electronic device therapy, have culminated in a growing cohort of patients with CHD who survive well into adulthood.[335] Arrhythmias increase in prevalence as adults with CHD age, are the most frequent reason for hospital admission, and, along with heart failure, are the leading cause of death.[336,337] A spectrum of arrhythmias may be encountered in adults, including pregnant women with CHD, with several types often coexisting. Bradyarrhythmias may involve disorders of the sinus node, AV node, His-Purkinje system, or intra-atrial propagation, and are often associated with tachycardias in bradycardia-tachycardia syndrome. About 50% of patients with CHD will develop an atrial tachyarrhythmia by the time they reach young adulthood.[338] Ventricular arrhythmias are the most frequent cause of sudden death in several types of CHD, with an overall risk up to 100-fold higher than age-matched controls.[339]

Recommendations for arrhythmia management in the pregnant patient with congenital heart disease

COR	LOE	Recommendations	References
1	B-NR	**1. Patients with CHD and arrhythmias who are considering pregnancy should receive preconception counseling, with input from an adult congenital cardiologist or electrophysiologist with expertise in adult CHD to determine maternal cardiac, obstetric, and fetal risks.**	46,331
1	B-NR	**2. Patients with Fontan circulation and refractory arrhythmias who are contemplating pregnancy should be advised that pregnancy is potentially harmful until the arrhythmias are addressed, due to the association with adverse maternal and fetal outcomes.**	340-343
1	C-LD	**3. In pregnant patients with CHD and intra-atrial reentrant tachycardia (IART), AF, or AFL, therapeutic anticoagulation regimen specific to pregnancy is recommended for stroke prevention.**	226,344-346
1	C-LD	**4. In pregnant patients with CHD and highly symptomatic or poorly tolerated acute onset IART, AF, or AFL, attempts to restore sinus rhythm (rhythm control) are recommended in preference to rate control only.**	226,333,344,347-349
1	C-LD	**5. In pregnant patients with complex CHD and hemodynamically unstable cardiac arrhythmias, urgent or emergency cardioversion is recommended as in the nonpregnant patient.**	38,155,159
1	C-LD	**6. In pregnant patients with CHD and recurrent VT, antiarrhythmic drug therapy should be tailored according to the underlying cardiac substrate and potential impact of the drug on the developing fetus, and preferably in conjunction with an electrophysiologist with expertise in CHD.**	285,333

(*Continued*)

Recommendations for arrhythmia management in the pregnant patient with congenital heart disease (*Continued*)

COR	LOE	Recommendations	References
2a	B-NR	7. In pregnant patients with CHD and recurrent IART, AF, or AFL, in whom a rhythm-control strategy is deemed necessary, it is reasonable to initiate antiarrhythmic drug therapy, alone or in combination with a beta-blocker, with the antiarrhythmic drug chosen according to the underlying cardiac substrate and potential impact of the drug on the developing fetus, and preferably in conjunction with an electrophysiologist with expertise in CHD.	45,226,333
2a	C-LD	8. In pregnant patients with CHD and recurrent atrial arrhythmias in whom pharmacological therapy is ineffective or contraindicated, ablation of arrhythmias deemed to involve a simple arrhythmic substrate is reasonable with attention to and techniques for eliminating or minimizing radiation exposure to as low as reasonably achievable, and preferably in conjunction with an electrophysiologist with expertise in CHD.	350
2b	C-LD	9. In pregnant patients with CHD and recurrent ventricular or atrial arrhythmias in whom other pharmacological or catheter ablation therapies are ineffective, contraindicated, or not preferred, amiodarone may be considered after a risks-versus-benefits discussion with the patient.	45,226,351
2b	C-LD	10. In pregnant patients with CHD and recurrent IART, AF, or AFL, in whom pharmacological therapy is ineffective or contraindicated, catheter ablation of arrhythmias deemed to involve a complex arrhythmic substrate may be considered, with attention to and techniques for eliminating or minimizing radiation exposure to as low as reasonably achievable, and preferably in conjunction with an electrophysiologist with expertise in CHD.	352

Synopsis

Preconception counseling and anticipatory management before pregnancy is important for all patients with CHD starting in childhood, and ideally arrhythmias should be managed prior to pregnancy. In general, anticoagulation for atrial arrhythmias is the same as in nonpregnant patients. In highly symptomatic patients with atrial arrhythmias, a rhythm control strategy is generally pursued, and cardioversion can be administered safely when patients are unstable or refractory to pharmacological therapy. When pharmacological therapy is necessary, the drug of choice depends on the underlying individual substrate, but drugs with the longest record of safe use during pregnancy are generally first-line agents. When arrhythmias are refractory to medical therapy, catheter ablation remains an option. Amiodarone is generally reserved for refractory cases, balancing benefits versus potential risks of side effects to the fetus. An algorithm of recommendations for the management of pregnant patients with CHD is shown in Figure 14.

Recommendation-specific supportive text

1. Patients with CHD are at higher risk of maternal and fetal complications, morbidity, and mortality during pregnancy than individuals without heart disease,[46,332] and Drenthen et al[331] noted that the most common complications of pregnant patients with CHD include arrhythmias and heart failure. Thus, it is important to have clear discussions regarding risks of pregnancy and to take steps to mitigate these risks with patients who have CHD and arrhythmias before they become pregnant.
2. A systematic review by Garcia Ropero et al[343] demonstrated that supraventricular arrhythmia was the most common adverse event in pregnant patients with Fontan circulation (8.4% of pregnancies with a range of 3-37%), and that supraventricular arrhythmias were generally managed successfully using conventional approaches. Refractory, persistent arrhythmias, however, are associated with poor fetal outcomes, and pregnancy may limit options for medications. Thus, it is optimal to address arrhythmias prior to pregnancy.
3. Patients with CHD are known to be at increased risk of thrombosis and thromboembolism, particularly in the setting of AF, AFL, and IART. Maternal CHD in particular increases maternal risk of thrombosis both during pregnancy and in the postpartum period. Thrombosis risk in the immediate postpartum period is as much as 4-fold higher than in the antepartum period.[226,344-346] For specific guidance on anticoagulation in pregnancy, see Recommendation 4 in Section 7.2, and Table 7.
4. Atrial arrhythmias are common in patients with CHD. IART is by far the most common (61% of patients), though among older patients AF that eventually progresses to permanent AF becomes more frequent.[353] In general, patients with CHD tolerate arrhythmias poorly, and LV function often suffers.[349] Salam et al[226] demonstrated that maternal mortality and low birth weight, but not heart failure, were higher in pregnant patients with

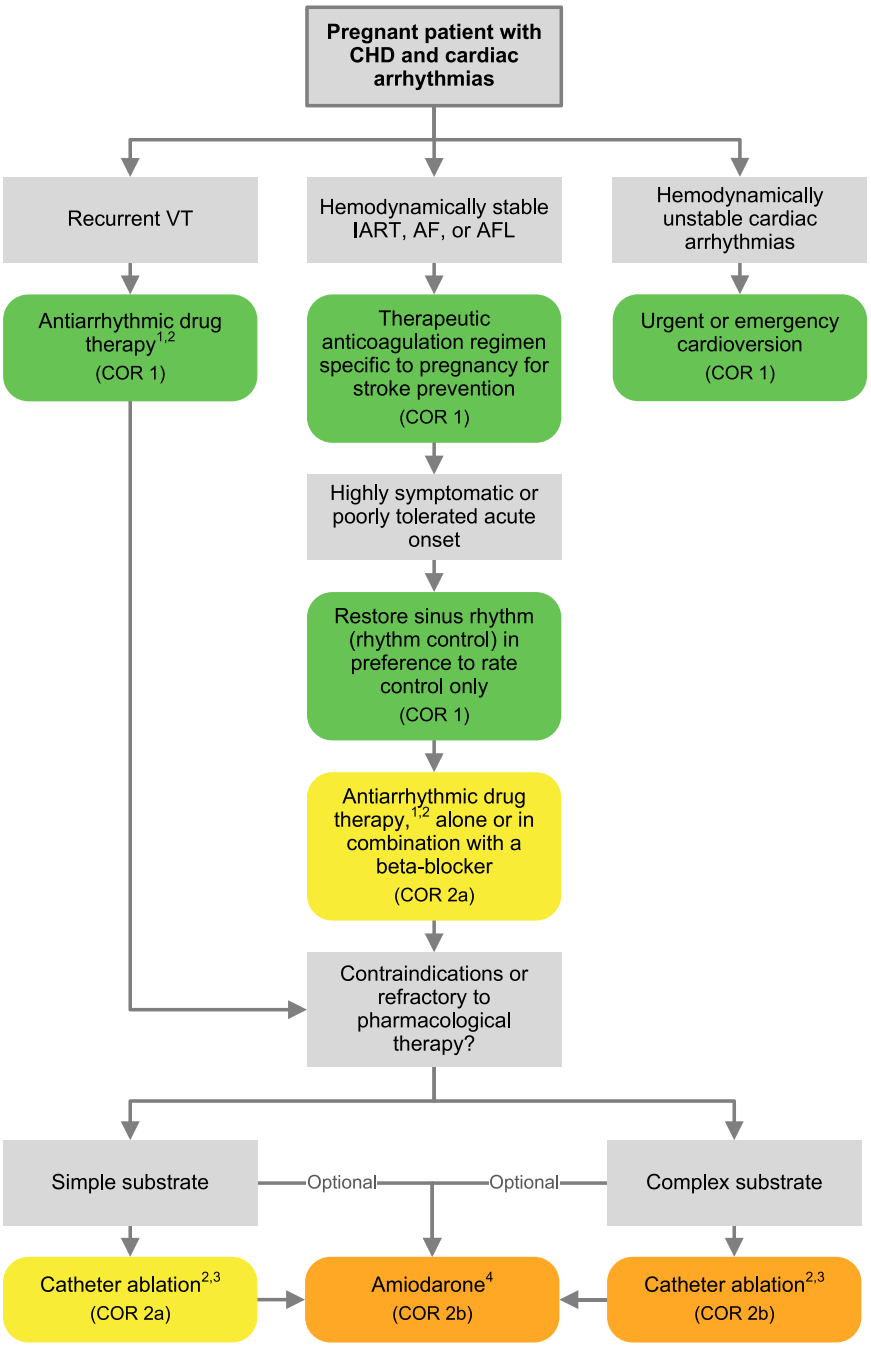

Figure 14 Management algorithm for pregnant patients with congenital heart disease (CHD). Colors correspond to class of recommendation (COR) in Table 1. [1]Arrhythmic drug chosen according to the underlying cardiac substrate and potential impact of the drug on the developing fetus. [2]Preferably in conjunction with an electrophysiologist with expertise in CHD. [3]With attention to and techniques for eliminating or minimizing radiation exposure to as low as reasonably achievable. [4]After a risks-versus-benefits discussion with the patient. AF = atrial fibrillation, AFL = atrial flutter, IART = intra-atrial reentrant tachycardia, VT = ventricular tachycardia.

CHD who had atrial arrhythmias. This association suggests that maintaining sinus rhythm during pregnancy may be associated with improved outcomes. There is a lack of studies reviewing the relative benefit of rate versus rhythm control for atrial arrhythmias during pregnancy. However, extrapolating from studies in nonpregnant patients, the association of arrhythmias with poor outcomes suggests that maintenance of sinus rhythm can offer benefit.

5. In pregnant patients who are unstable due to ongoing arrhythmia, restoration of normal rhythm to protect both the mother and the fetus is critical. Arrhythmias

are particularly common in the setting of CHD. There is no obvious difference in risk conferred by cardioversion in patients with CHD compared with those without, and cardioversion is generally well tolerated in pregnancy.[155,159] Refer to Section 4.1 for a full discussion of cardioversion in pregnancy.

6. VT during pregnancy is associated with maternal morbidity and mortality, and can also result in negative fetal outcomes. Overall, VT during pregnancy is uncommon, occurring in 1.4% of pregnancies and mainly during the third trimester.[285] However, when VT is observed during pregnancy, the presence of heart failure is more likely, and there is a higher risk of maternal mortality, neonatal death, and preterm birth. Tateno et al[333] demonstrated that VT is not uncommon among patients with CHD (9 of 31 patients). Thus, given potential associated negative outcomes, efforts to prevent VT during pregnancy in congenital patients are important. However, the choice of therapy should take into account underlying substrate and potential fetal effects.
7. IART, AFL, or AF are common in CHD, and thus many patients with CHD will have a history of atrial arrhythmias prior to pregnancy. Silversides et al[45] demonstrated that 44% of patients with preexisting arrhythmias have recurrent episodes during pregnancy. Recurrence rates are highest for SVT and AF/AFL. Adverse fetal events may occur more frequently in the setting of arrhythmias. Thus, arrhythmia control can offer some benefit. Beta-blockers may offer some antiarrhythmic benefit in pregnancy and have a long record of safety when administered to pregnant women. If beta-blockers are not effective or result in excessive symptoms, antiarrhythmic drugs can be an effective treatment. However, given the potential variable risks of antiarrhythmic drugs to the fetus, clear discussion should be had with the patient about fetal and maternal risks. In general, drugs with a longer record of safety during pregnancy are preferred.
8. During pregnancy, ablation without use of fluoroscopy has been shown to be feasible.[350] Driver et al[243] have also suggested that ablation of arrhythmias in CHD is both feasible without X-ray and effective. However, consideration should be made of the substrate and the nature of the arrhythmia. For example, AV nodal reentry tachycardia and accessory pathways are associated with higher success rates. However, AV nodal reentry tachycardia in congenitally corrected transposition of the great arteries can be associated with higher complexity. Therefore, consideration of both the substrate and the arrhythmia to be ablated is needed prior to proceeding with an ablation strategy.
9. While amiodarone is an effective antiarrhythmic for many arrhythmias, it is associated with a risk of fetal abnormalities. Up to 17% of neonates may develop hypothyroidism and some evidence of neurotoxicity.[126] Thus, use of amiodarone is generally limited to instances of refractory or life-threatening arrhythmias that cannot be controlled with other medications, and requires close monitoring for potential side effects. Shared decision-making with the mother in advance of therapy initiation includes discussion of potential long-term risks to mother and fetus.
10. IART, AFL, and AF may be amenable to ablation in CHD.[352] In the setting of pregnancy, ablation is complicated by the need for avoiding use of X-ray and the more complex substrate associated with ablation of IART, AFL, AF, particularly in the setting of complex CHD. Thus, ablation strategies should be seen as a last-line option, after either pharmacologic failure or contraindication. In addition, ablation should be done at centers experienced with ablation in CHD and with minimizing fluoroscopy use.

10.3. Arrhythmia management in the pregnant patient with valvular heart disease

The increase in plasma volume, heart rate, and cardiac output during pregnancy can lead to cardiac complications in women with valvular heart disease. In women of childbearing age, valvular heart disease is usually diagnosed prior to pregnancy, but it may also be identified for the first time during pregnancy. The most common valve lesions in women of childbearing age are aortic stenosis and mitral stenosis. Aortic stenosis is usually due to bicuspid aortic valve disease. There have been a number of case series of pregnancy outcomes in women with aortic stenosis reporting variable rates of complications.[40,354] In a meta-analysis, new or recurrent tachyarrhythmias occurred in 2% and 4% of pregnancies in women with moderate or severe aortic stenosis, respectively.[355] Women with aortic stenosis are also at risk for developing heart failure during pregnancy, and these women are also at risk for developing VT.

Mitral stenosis is usually due to rheumatic heart disease and is much more common in developing countries. Reported rates of complications in pregnant women with mitral stenosis have considerable geographical variability.[40,354,356,357] In a meta-analysis of pregnancy outcomes in medium and higher Human Development Index countries, new or recurrent atrial tachyarrhythmias during pregnancy occurred in 5% and 16% of pregnancies in women with moderate or severe mitral stenosis, respectively.[355] Management of anticoagulation during pregnancy is more complex than in the nonpregnant popula-

tion due to the potential fetal effects of warfarin (warfarin embryopathy and warfarin fetopathy) and the risk of bleeding at the time of delivery and early postpartum.[358] Direct oral anticoagulants are not used during pregnancy because safety data are not available. Low-molecular-weight heparin does not cross the placenta and for that reason is an acceptable alternative to warfarin during pregnancy. Refer to Table 7 for specific guidance on anticoagulation in pregnancy.

Recommendations for arrhythmia management in the pregnant patient with valvular heart disease

COR	LOE	Recommendations	References
1	C-LD	1. In pregnant patients with mitral stenosis and acute onset of either AF or AFL of any duration, synchronized cardioversion is recommended, as long as the patient is adequately anticoagulated or atrial thrombus is excluded, and subsequent anticoagulation will be provided with the duration as in the nonpregnant patient.	40,354,356,359,360
1	C-LD	2. In pregnant patients with mitral stenosis and either AF or AFL, left atrial thrombosis, or prior embolism, therapeutic anticoagulation is recommended throughout pregnancy, unless there is contraindication.	40,354,356

Synopsis

Atrial tachyarrhythmias can precipitate heart failure and can also lead to thromboembolic complications, often secondary to left atrial thrombus. Beta-blockers, which slow the heart rate and prolong the diastolic filling time, are the mainstay of therapy for both prevention and treatment of acute AF and flutter.[40,354,356] Women with mitral stenosis who are taking beta-blockers prior to pregnancy should continue their beta-blockers during pregnancy. As part of a rhythm control strategy, cardioversion is deemed safe during pregnancy. All women with mitral stenosis and AF or AFL benefit from therapeutic anticoagulation during pregnancy as in the nonpregnant population.

Recommendation-specific supportive text

1. AF and AFL are common cardiac complications in pregnant women with mitral stenosis, especially if moderate or severe, that predispose them to left atrial thrombus, particularly when the duration of the arrhythmias is prolonged beyond 48 hours. In general, these arrhythmias are poorly tolerated, which is why rhythm control strategies might be necessary. When cardioversion is being considered, the patient must be adequately anticoagulated unless the arrhythmia is <48 hours in duration. For women with longer duration arrhythmias or in whom the duration of arrhythmia is unknown, a transesophageal echocardiogram to exclude left atrial thrombus is performed. In addition, anticoagulation is provided for a minimum of 4 weeks post-cardioversion, as in the nonpregnant population.[26,359]
2. Pregnancy is a prothrombotic state and is associated with increased risk of thromboembolic complications. During pregnancy, women with mitral stenosis and AF or AFL are at particularly high risk for developing thromboembolic complications.[361] Anticoagulation recommendations for pregnant patients with mitral stenosis, AF, and AFL are similar to the nonpregnant state.[362] Additionally, pregnant patients with a prior thromboembolic complications or documented left atrial thrombus are managed with the same therapeutic anticoagulation approach. Refer to Table 7 for anticoagulation in pregnancy protocols.

10.4. Arrhythmia management in the pregnant patient with arrhythmogenic cardiomyopathy

ACM is an inherited cardiomyopathy with a prevalence of 1:2000 to 1:5000. Although first defined as characterized by fibro-fatty replacement of the right ventricular myocardium, which predisposes patients to ventricular arrhythmias, right ventricular dysfunction, and sudden cardiac death, recognition has increasingly widened to include LV involvement, accounting for the change in nomenclature from ARVC (arrhythmogenic right ventricular cardiomyopathy) to ACM.[10,150,363] Diagnosis of ACM is made using a set of criteria that includes clinical presentation and diagnostic modalities. Inheritance of ACM is autosomal dominant with reduced penetrance and marked variable expressivity, and affected genes are those encoding the cardiac desmosome.[10,363]

Recommendations for the arrhythmia management of the pregnant patient with arrhythmogenic cardiomyopathy			
COR	LOE	Recommendations	References
1	B-NR	1. Patients and/or their partners with ACM should be offered preconception counseling, including genetic counseling as indicated.	150-152
1	C-LD	2. Pregnant patients with ACM should be treated for documented or potential arrhythmias as in the nonpregnant patient, including continuation of beta-blockers and the use of antiarrhythmic drug– and device-based therapies as needed, favoring options with the best record of safety during pregnancy.	150,152,364,365
1	C-LD	3. In pregnant patients with ACM and high-risk features, the decision to implant an ICD should be made based on usual indications, regardless of pregnancy status, and ideally the procedure should be considered and performed prior to conception.	150,152,269
2a	C-LD	4. In pregnant patients with ACM and recurrent VT or ICD shocks, it is reasonable to consider antiarrhythmic drug therapy, including sotalol or flecainide alone or in combination with a beta-blocker as first-line options.	150,152

Synopsis

Evidence demonstrates that in patients with ACM, pregnancy is generally well tolerated, yet cardiac adverse events, such as ventricular arrhythmias and heart failure, can be observed, especially in high-risk patients. Antiarrhythmic drug therapy is generally well tolerated. Preconception genetic counseling, implantation of ICD if clinically indicated, and evaluation of cardiac function are ideal for the sake of better risk stratification and management.

Recommendation-specific supportive text

1. In ACM, approximately 50-60% of patients will have an identifiable pathogenic mutation associated with the cardiac desmosome.[10,151,363,366] Yet, genetic counseling is complicated by the fact that there is great variable expressivity and reduced penetrance, even within members of the same family, and by the fact that some patients can be compound heterozygotes, or carry more than 1 mutation. In addition, common sequence variants with high prevalence in healthy controls can act as modifiers in ACM.[10,366] Therefore, preconception counseling of a woman or couple with ACM requires expertise in the complexities of genetic testing in ACM and cardiomyopathies in general.[151,363]
2. A number of observational studies and data from registries have shown that pregnancies in patients with ACM are generally uneventful with optimal surveillance and therapy. One study identified the third trimester of the pregnancy and the puerperium as high-risk periods for ventricular arrhythmias.[364] The largest experience was published by Hodes et al,[150] who used data from a combined registry that included 39 pregnancies. Though they concluded that pregnancy was generally well tolerated, with positive fetal outcomes and no cardiac mortality, sustained ventricular arrhythmias were reported in 13% and heart failure in 5% of pregnancies, respectively. In the 2 pregnancies during which heart failure was reported, both patients had prior-documented significant structural impairment.[150] In this cohort, common drugs were sotalol, flecainide, and beta-blockers, and the majority had ICDs implanted previously. Of note, beta-blocker use was associated with low birth weight.[150] Pregnancy does not seem to worsen the ACM phenotype over the long term.[365]
3. Decisions regarding a primary or secondary prevention ICD in a pregnant woman with ACM are guided by the usual decision-making process, not the pregnancy status. The procedure has been shown to be generally safe during pregnancy with negligible risk from radiation exposure in a small number of reports. Pregnancy subsequent to ICD insertion is a more frequently described and well tolerated situation.[269] In the studies by Hodes et al[150] that included 39 pregnancies, most patients had ICDs, and excess arrhythmia burden or shocks were not observed generally.
4. In the largest study, Hodes et al[150] reported that although pregnancy was generally well tolerated, sustained ventricular arrhythmias were seen in 13% of the cohort. The 2 antiarrhythmic drugs used most commonly were flecainide and sotalol. Both drugs have a long record of safety in pregnancy, as both are well tolerated and drugs of choice for fetal SVT. In addition, both drugs, alone or in combination, have been used successfully in nonpregnant ACM cohorts.[367,368] Amiodarone appears to be superior to sotalol, yet in view of risk of toxicity, it is best used as a last resort.[369]

10.5. Arrhythmia management in the pregnant patient with hypertrophic cardiomyopathy

HCM is one of the most common inherited forms of cardiomyopathy. The presentation is quite heterogeneous, yet most patients have favorable long-term outcomes with contemporary therapies and early diagnosis. In view of the increased hemodynamic demands associated with pregnancy, the safety of pregnancy in HCM has been an important question.

Recommendations for arrhythmia management of the pregnant patient with hypertrophic cardiomyopathy			
COR	LOE	Recommendations	References
1	B-NR	1. Women and/or their partners with HCM should be offered preconception counseling, including genetic counseling.	370,371
1	C-LD	2. Pregnant patients with HCM should be treated for documented or potential arrhythmias as in the nonpregnant patient, including continuation of beta-blockers and the use of antiarrhythmic drug– and device-based therapies as needed, favoring options with the best record of safety in pregnancy.	372-376

Synopsis

A number of studies have shown generally good pregnancy outcomes among patients with HCM, although complications are observed especially in those previously identified as high risk.[372] The third trimester appears to be a particularly high-risk period. Potential and documented maternal arrhythmias are generally treated as in the nonpregnant state, favoring therapeutic options with a record of safety in pregnancy.

Recommendation-specific supportive text

1. Prenatal counseling can help parents understand the risk of transmission of heritable diseases, including HCM, and the risks of pregnancy for the mother and the baby. Genetic counseling can introduce options including, but not limited to, prepregnancy genetic diagnosis, fetal screening, maternal and paternal prenatal testing, and postnatal testing for the infant and family. The potential benefits, risks, and alternatives should be discussed for all of these options during preconception counseling, such that the patient or parents can make a fully informed decision about pregnancy, prenatal genetic testing, and fetal screening.[6,370,371,377,378]
2. Autore et al[372] reported their experience with 100 women with HCM who had a total of 199 births. They concluded that, despite higher maternal mortality in patients with HCM compared with the general population, absolute maternal mortality was low and confined to women at a particularly high risk. The progression of symptoms, AF, and syncope was uncommon during pregnancy. Data from the ROPAC registry[376] showed that despite overall good outcomes, 23% of pregnant women with HCM developed major cardiac events, including VT in 10% and AF in 1.7%. A particularly high-risk period was the third trimester, and most events occurred in patients already identified as high risk prior to pregnancy. Schinkel[375] performed a systematic review of 11 studies, which included 237 women and 408 pregnancies, finding that, although the overall event rate was low, the maternal mortality rate was 0.5%, and complication or worsening of symptoms occurred in 29%. Across these studies, maternal arrhythmias were generally treated with standard therapies, and the great majority of patients were maintained on beta-blockers throughout the pregnancy.

Section 11 Management of fetal arrhythmias

The normal fetal heart rate range is between 110 and 160 bpm. If the heart rate is beyond the normal range or the rhythm is irregular, then a fetal arrhythmia is detected. It is also possible to have a fetal arrhythmia that is regular and falls in the normal heart rate range, but these normal-rate dysrhythmias will often go undetected until after birth. The heart rate, duration, mechanism of the rhythm and degree of irregularity usually predict the hemodynamic consequences. Fetal arrhythmias are diagnosed in approximately 1% of all fetuses and up to 49% of referrals for fetal echocardiograms.[379] This section covers general fetal arrhythmias not related to IAS, which are covered in Section 12.2.

11.1. Fetal atrial tachyarrhythmias

While intermittent atrial tachyarrhythmias in the fetus have an excellent prognosis, fetuses with sustained tachycardias are at increased risk of stillbirth and morbidity.[380] Incessant (in tachycardia >50% of the time or >12 hours per day) fetal SVT is often associated with fetal hydrops and ventricular dysfunction.[380] AFL accounts for approximately 30% of all fetal tachyarrhythmias and is often associated with CHD.[232] Incessant (>50% of the time or greater than 12 hours per day) fetal AFL is often accompanied by fetal hydrops and ventricular dysfunction, and resultant neurologic sequelae and mortality (5-30%).[78,380,381] In the setting of fetal arrhythmias, the cardio-obstetrics team in the context of the management of the fetus should include, if available, a fetal or pediatric cardiologist or electrophysiologist, perinatologist (maternal-fetal medicine subspecialist), and neonatologist.

Recommendations for fetal atrial tachyarrhythmias			
COR	LOE	Recommendations	References
1	B-NR	1. Fetuses with intermittent AFL or intermittent SVT (defined as tachycardia <50% of the time) and no hydrops should be managed with observation, frequent fetal heart rate monitoring (auscultation), and serial biophysical testing, ideally under the guidance of a cardio-obstetrics team.	74,232,381
1	B-NR	2. Fetuses with incessant AFL or incessant SVT (defined as tachycardia >50% of the time) and/or hydrops should be referred to a cardio-obstetrics team, due to the potential for high fetal and maternal morbidity and fetal mortality.	232,381,382
1	B-NR	3. Fetuses with incessant SVT or AFL with or without hydrops who are not considered to be mature enough for delivery should be treated transplacentally with flecainide or sotalol, alone or in combination with digoxin, with frequent monitoring of fetal well-being and maternal drug toxicity, and with drug selection according to the specific arrhythmia mechanism.	78,80,108,383,384
1	C-LD	4. Fetuses with incessant AFL or incessant SVT complicated by hydrops who are close to term should be delivered.	381,385,386
1	C-LD	5. In pregnancies complicated by either fetal irregular heart rate or tachyarrhythmias, fetal echocardiography is recommended to further characterize the rhythm and to screen for structural or functional abnormalities.	387,388
1	C-LD	6. In pregnancies complicated by fetal PACs, serial auscultation of the fetal heart rate or serial biophysical testing (or, if these are unavailable, non-stress testing) is recommended to exclude development of fetal SVT until the arrhythmia resolves.	388
2a	C-LD	7. In fetuses with incessant SVT complicated by hydrops or ventricular dysfunction refractory or with contraindications to first-line drug options, transplacental administration of oral amiodarone can be beneficial.	127,128
2a	C-LD	8. In immature fetuses with incessant SVT or incessant AFL complicated by hydrops that do not respond to treatment with transplacental drug therapy alone, direct fetal intramuscular injection of digoxin added to transplacental drug therapy can be effective.	97
2b	C-LD	9. In fetuses with incessant SVT or incessant AFL complicated by hydrops that do not respond to treatment with transplacental drug therapy, combination transplacental drugs, or direct injection of digoxin, direct umbilical intravenous injection or intraperitoneal injection of amiodarone may be effective as a last resort.	389-392
3: Harm	C-LD	10. In fetuses with incessant SVT or incessant AFL, transplacental therapy with verapamil is potentially harmful.	393,394

Synopsis

The management of fetal atrial tachyarrhythmias depends on gestational age, evidence of fetal hydrops, and potential risk to the mother. In the fetus noted to have SVT on auscultation of the fetal heart rate, it is important to assess the mechanism of tachycardia, as well as tachycardia burden, and to involve a cardio-obstetrics team (see Sections 1.10 and 3.2) in the development of a treatment plan. Flecainide has been found to be a superior first-line agent in fetal SVT, followed by digoxin and sotalol.[108] In fetuses with recalcitrant SVT, multiple drug regimens or the addition of direct intraperitoneal or umbilical medication administration are often used.[78,97,108,127,128,383,384,389,390] Digoxin or sotalol are considered the first line for management of AFL in fetuses with hemodynamic compromise.[78,108,383] Due to the potential for adverse events, when pharmacological therapy is required to treat fetal tachyarrhythmias, a full discussion between the physician and parents about the maternal and fetal risks and benefits enables joint decision-making. Additionally, careful monitoring of mother and fetus is necessary to avoid drug toxicity and side effects. Delivery of fetuses diagnosed with incessant AFL or incessant SVT close to term, if deemed viable, generally results in better outcomes. An algorithm for the management of fetal tachyarrhythmias is shown in Figure 15.

Recommendation-specific supportive text

1. Several case reports and nonrandomized retrospective studies have found that intermittent AFL (<50% of the time or <12 hours per day) in fetuses with no evidence of hydrops on fetal ultrasound or fetal echocardiogram is well tolerated with good outcomes.[232,381] Cuneo and Strasburger[74] found that in 15 fetuses with intermittent tachycardia, none progressed to sustained tachycardia or heart failure. Management of intermittent AFL with frequent monitoring is generally sufficient and is less risky to the mother than drug therapy.

2. In contrast to fetuses with intermittent AFL or SVT, those with incessant AFL, incessant SVT (defined as tachycardia for >50% of the time or >12 hours per day), or hydrops have worse outcomes, with increased risk of mortality and morbidity.[232,381,382] Therefore, pharmacological therapy is often necessary for these pregnancies. First-line therapy is transplacental and exposes the mother to the side effects and risks of antiarrhythmics. Therefore, management of the mother and fetus by a cardio-obstetrics team (see Sections 1.10 and 3.2) is optimal. In this context a pediatric cardiologist, or a pediatric electrophysiologist, if available, is an integral multidisciplinary team member.
3. A number of studies have compared different drugs for transplacental therapy of fetal SVT. Sridharan et al[384] compared flecainide and digoxin in a nonrandomized study involving 84 patients; flecainide was superior to digoxin especially when hydrops was present. A meta-analysis of 10 studies and 537 patients found flecainide to be superior to digoxin and sotalol, with the relative effectiveness of flecainide over digoxin even more apparent once hydrops was present with SVT in general.[108] In the same study, a trend toward a higher arrhythmia termination rate was observed for flecainide versus sotalol. Data are conflicting as to whether digoxin or sotalol therapy is superior to treat specifically fetal AFL and/or hydrops. Jaeggi et al[78] performed a multicenter, nonrandomized trial of antiarrhythmics in fetuses with AFL, finding sotalol to be a superior therapy for fetuses with incessant flutter. However, a systemic review and meta-analysis of studies of fetuses with AFL found no difference when comparing sotalol and digoxin therapies.[108] Thus, no data strongly indicate a preferred first-line agent for AFL; however, some studies suggest a better arrhythmia termination rate with sotalol. A high number of maternal adverse events from transplacental antiarrhythmics have been reported (although the majority of maternal side effects are not serious).[80] Therefore, the choice of pharmacological therapy depends on a full discussion of the risks and benefits with the family.
4. Infants with AFL with or without hydrops respond well to cardioversion, with a low risk of recurrence.[385] Hinkle et al[386] found that infants with refractory SVT or hydrops did not have a higher risk of postnatal SVT. Therefore, the delivery of a close-to-term fetus with incessant AFL or incessant SVT with hydrops allows for optimal therapy and also avoids the potential for maternal side effects due to pharmacological therapy. Importantly, neonatal morbidity from hydrops may be reduced if rapid conversion is achievable. Certainly, the decision should be based on considerations such as gestational age, presence of hydrops, and response to therapy. The presence of hydrops requires a higher level of urgency. The term *close to term* is purposely vague, as defined in Section 1.10; in this instance, it refers to the fact that the fetus is deemed viable.
5. Irregular or rapid heart rate may be a sign of significant arrhythmia in the fetus and may be associated with CHD or poor function.[25,76,388] Fetal echocardiography helps to determine arrhythmia etiology. Copel et al[388] reported their experience with 595 cases referred for fetal irregular rhythms, with 2.4% of these presenting with hemodynamically significant arrhythmias.
6. PACs are a common finding in the fetus and are usually benign. However, monitoring by serial weekly fetal "doppler" auscultation can identify intermittent runs of SVT, which is seen in 1-3% of fetuses and could potentially lead to fetal compromise.[76] This may be discontinued 1-2 weeks after resolution of the arrhythmia or until delivery.
7. Transplacental amiodarone has been shown to be a successful treatment for drug-refractory SVT.[127,128] Strasburger et al[128] found that amiodarone, either alone or in combination with other drugs, converted 14 out of 15 of fetuses with SVT. Amiodarone-related adverse effects were transient in 5 infants and 9 mothers. Of note, the time to therapeutic effect with amiodarone may be longer than with other antiarrhythmics; thus, close monitoring is essential to detect worsening hydrops and an abnormal biophysical profile.
8. Maternally administered digoxin for the treatment of fetal SVT and AFL is less effective when hydrops is present, as transplacental drug transfer is impaired. Parilla et al[97] reported successful conversion in 8 fetuses with combined maternal and direct fetal intramuscular digoxin therapy.
9. Hansmann et al[389] reported on 13 fetuses with refractory SVT and AFL complicated by hydrops, who received intraperitoneal and/or umbilical intravenous administrations of a number of drugs in addition to the transplacental therapy. Amiodarone was the most effective drug, and the authors described it as the first drug of choice for direct therapy.[389] Direct amiodarone injections into the fetal peritoneal cavity has also been performed successfully.[390] The risks and benefits of a direct intrafetal injection versus preterm delivery must be made on a case-by-case basis depending on gestational age.
10. A number of adverse outcomes have been reported with the use of verapamil in both the mother and the fetus.[25,75] These include maternal hypotension and bradycardia, as well as fetal bradycardia, hypotension, depression of cardiac contractility, and asystole. Unexpected fetal death associated with the use of verapamil has been reported, although certainly other factors could have come into play and numbers are small.[393] Reports of effective SVT termination with verapamil do exist, especially when combined with digoxin. Nevertheless, in view of concerning reports about the safety of verapamil and the availability of safer and more effective pharmacological options for fetal SVT and AFL, verapamil is best avoided for fetal SVT (Table 5).

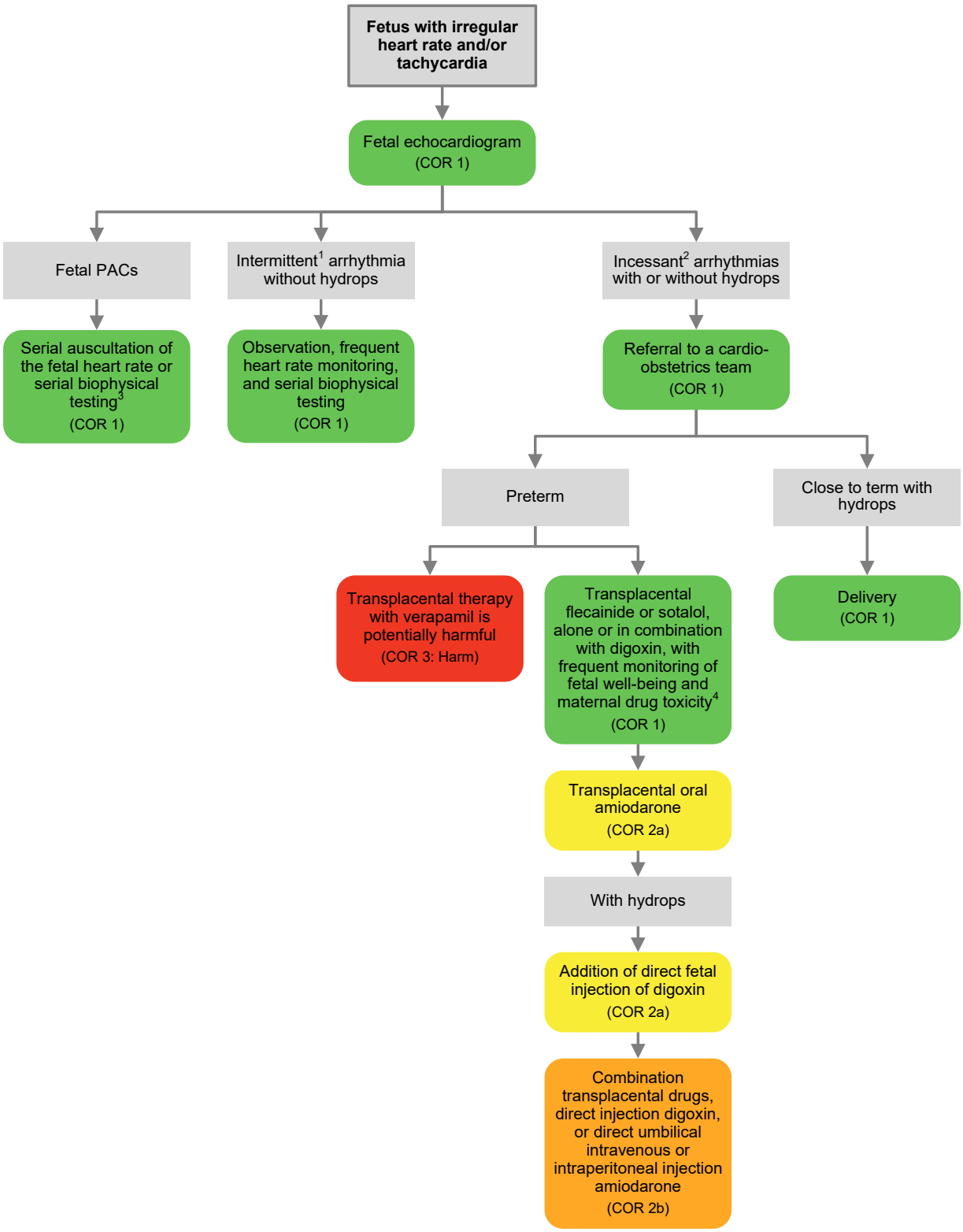

Figure 15 Management of fetuses with irregular heart rate and tachycardia. Colors correspond to the class of recommendation (COR) in Table 1. [1]*Intermittent* is defined as <50% of the time. [2]*Incessant* is defined as >50% of the time. [3]If these are unavailable, nonstress testing is recommended. [4]Drug selection according to the specific arrhythmia mechanism. The term *close to term* is purposely vague, as defined in Section 1.10, but it implies likely viability after delivery. PAC = premature atrial contraction.

11.2. Fetal ventricular arrhythmias not associated with inherited arrhythmia syndromes

While fetal ventricular arrhythmias most often are associated with IAS, specifically LQTS (see Section 12.2 for fetal arrhythmias secondary to IAS), ventricular arrhythmias in the fetus can have several other causes. Fetuses with AV block, cardiac tumors, myocarditis, ventricular aneurysms, and cardiomyopathy can all present with VT.[395-397] Accelerated idioventricular tachycardia, a generally benign rhythm of infancy, can also be seen in the prenatal period. Early involvement of a cardio-obstetrics team, including a pediatric electrophysiologist, is of great importance.

Recommendations for fetal ventricular arrhythmias not associated with inherited arrhythmia syndromes

COR	LOE	Recommendations	References
1	B-NR	1. Fetuses with sustained VT with or without hydrops who are not considered to be mature enough for delivery should be treated transplacentally with either intravenous magnesium or oral propranolol, mexiletine, or lidocaine, alone or in combination, or with other antiarrhythmic agents according to the specific arrhythmia etiology, with frequent monitoring of fetal well-being and maternal drug toxicity.	134,154,398
1	C-LD	2. In fetuses with sustained VT, maternal hypomagnesia and other correctable causes should be treated aggressively.	398
1	C-EO	3. Fetuses with VT should be referred to a cardio-obstetrics team, if available, for evaluation and treatment secondary to the high fetal morbidity and mortality.	
1	C-EO	4. Fetuses with sustained VT with or without hydrops who are close to term or at term should be delivered.	
2a	B-NR	5. In fetuses with VT complicated by hydrops or ventricular dysfunction refractory or with contraindications to first-line drug options and not secondary to IAS, transplacental administration of flecainide, sotalol, or amiodarone can be beneficial, with the choice of drug according to the underlying maternal and fetal substrate.	128,134,154
2b	B-NR	6. Fetuses with sustained VT suspected to be secondary to myocarditis or isoimmunization, depending on gestational age, may be treated with dexamethasone and/or intravenous immunoglobulin (IVIG).	395,399,400

Synopsis

VT in the fetus is an extremely rare occurrence but can be associated with hydrops and sudden fetal death. Therefore, referral to a cardio-obstetrics team, pharmacological therapy, or delivery of a close-to-term fetus may improve outcomes. An exception is accelerated idioventricular tachycardia, a generally benign rhythm seen in the prenatal period in healthy neonates, which in most cases does not require therapy, unless there is evidence of hydrops. The majority of fetuses who present with VT have an IAS, most commonly LQTS. Thus, most data on therapy refer to this population; therapy includes either maternal intravenous magnesium or oral propranolol, mexiletine, or lidocaine, alone or in combination. Treatment for VT not thought to be secondary to LQTS is generally extrapolated from the arrhythmia literature in the general population; as such, standard antiarrhythmic drugs such as sotalol, flecainide, and amiodarone are recommended. When VT is deemed to be secondary to myocarditis or isoimmunization, dexamethasone and IVIG are considered, although data are limited and conflicting. An algorithm of the recommendations for the management of fetal ventricular arrhythmias not associated with IAS is shown in Figure 16.

Recommendation-specific supportive text

1. In the majority of cases of sustained VT, the first-line therapy for the fetus includes maternal intravenous magnesium and lidocaine. Limiting maternal magnesium to <48 hours' duration[134] reduces the risk of maternal toxicity. Monitoring of magnesium levels is advisable, and magnesium may be redosed if there is recurrent VT as long as maternal magnesium levels are <6 mEq/L. In some reports, oral propranolol and mexiletine therapy have also been used as first-line agents for this indication.[128,134]
2. Simpson et al[398] described a case of a fetus presenting at 30 weeks' gestation with VT at a rate of 220 bpm and fetal hydrops. The tachycardia was unresponsive to flecainide but was controlled within 12 hours by an intravenous infusion of magnesium to the mother. In experimental prolonged QT interval canine models, magnesium has shown to be effective in treating LQTS.[401]
3. VT in the fetus can be due to a number of structural or genetic conditions.[395,399,400] Sustained VT in the fetus is associated with high morbidity and mortality. Therefore, pharmacological therapy is often necessary in these patients. First-line therapy is usually transplacental administration of drugs, which exposes the mother to the side effects and risks of antiarrhythmics. Consequently, management of the mother and fetus by a cardio-obstetrics team (see Sections 1.10 and 3.2) is optimal even in cases with intermittent tachycardia.
4. The efficacy of antiarrhythmic drugs delivered transplacentally can be limited, especially in the setting of hydrops. In the event of sustained VT in the close-to-term fetus, delivery and direct treatment by cardioversion or defibrillation, along with administration of antiarrhythmics, provide more effective drug delivery and avoid

exposure of the mother to potent antiarrhythmics. The exception is rapid and frequent polymorphic VT, in which stabilization of the arrhythmia through in utero therapy may be warranted prior to delivery. The term *close to term* is purposely vague, as defined in Section 1.10, but it implies likely viability after delivery.

5. Fetuses with VT refractory to first-line therapy have been found to be responsive to a number of antiarrhythmic drugs, including sotalol, flecainide, and amiodarone.[128,134,154,398] No one drug has been found to be superior to the others, and data are scant since these arrhythmias are rare, so drug options listed are based on the history of their use in pregnancy for other indications, such as fetal SVT. The drug choice also should be determined by arrhythmia severity and underlying maternal and fetal substrate. If the VT is suspected to be secondary to de novo LQTS or IAS, however, it is too risky to use these antiarrhythmic agents, as they all can prolong the QT interval.
6. Myocarditis in the fetus has been well described and can be associated with ventricular arrhythmias.[395,400] Dexamethasone and IVIG have been used as effective therapies in this entity in a limited number of case reports. Nevertheless, data on this entity are extremely limited and mixed, and the consideration of the use of dexamethasone in utero requires a full discussion of risks versus benefits of therapy to enable joint decision-making.

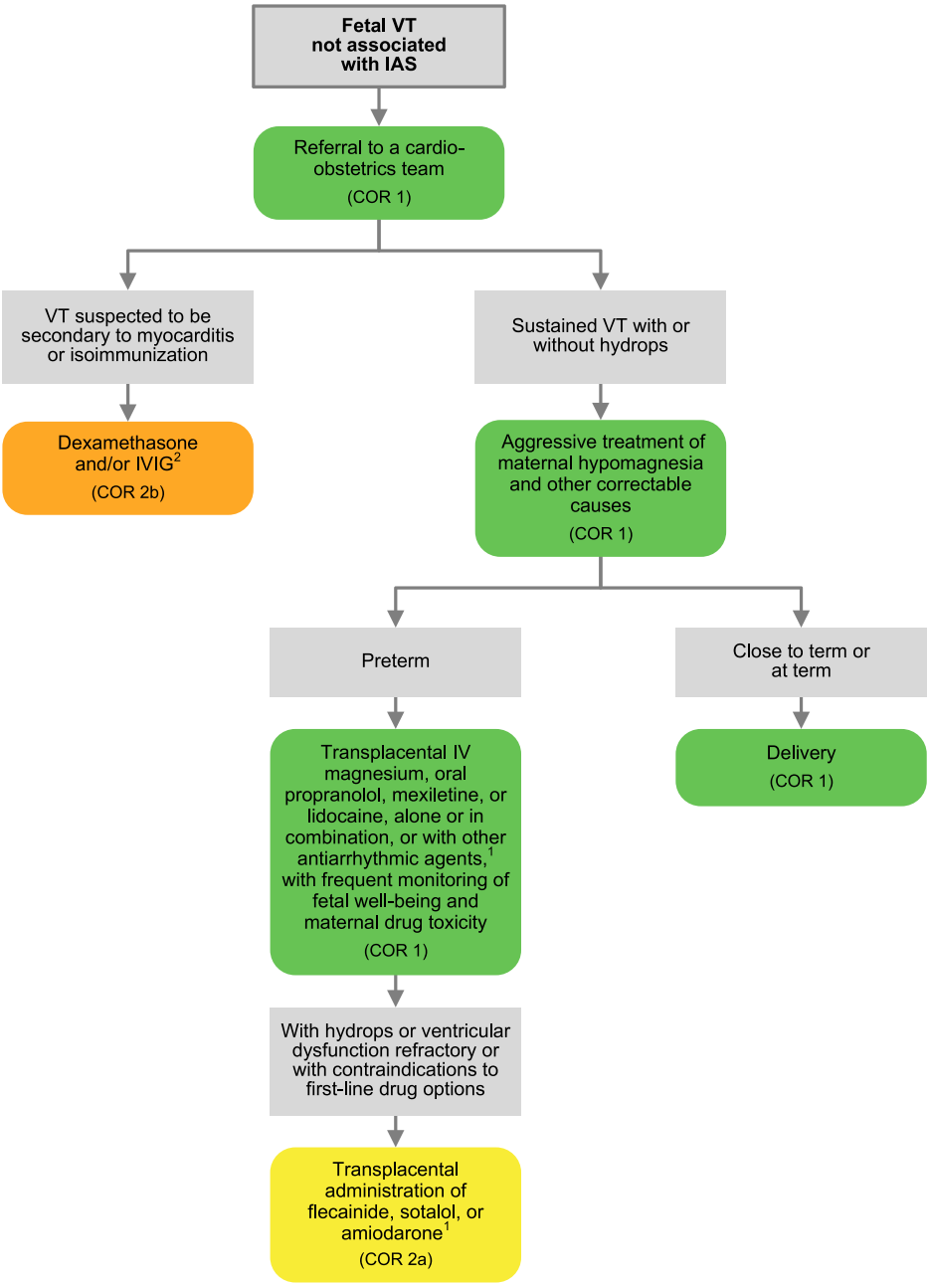

Figure 16 Algorithm for management of ventricular tachycardia (VT) in the fetus not secondary to inherited arrhythmia syndrome (IAS). Colors correspond to the class of recommendation (COR) in Table 1. [1]Choice of drug according to the arrhythmic etiology and/or underlying maternal-fetal substrate. [2]Depending on gestational age. The term *close to term* is purposely vague, as defined in Section 1.10, but it implies likely viability after delivery. IV = intravenous, IVIG = intravenous immunoglobin.

11.3. Management of fetal bradycardia conduction system disorders

Recommendations for the management of fetal bradycardia conduction system disorders			
COR	LOE	Recommendations	References
1	B-NR	1. Pregnant patients with autoimmune and rheumatological disease should be evaluated for anti-Ro and anti-La antibodies in the first trimester of pregnancy or when care is initiated, even if previous titers were negative.	402-404
1	B-NR	2. In pregnancies complicated by third-degree fetal heart block, echocardiographic monitoring is recommended for surveillance of fetal hydrops and cardiomyopathy, since these conditions can lead to fetal compromise or the need for delivery.	405,406
1	C-LD	3. In pregnancies complicated by fetal bradycardia, fetal echocardiography is recommended to further characterize the rhythm and to screen for structural cardiac abnormalities.	403
1	C-LD	4. In pregnancies complicated by idiopathic fetal bradycardia, antenatal and postnatal evaluation of the neonate for IAS is recommended.	407
1	C-EO	5. In pregnancies complicated by fetal bradycardia, assessment of fetal well-being as appropriate for gestational age is recommended to exclude fetal compromise.	
2a	C-LD	6. In pregnant patients with positive anti-Ro and anti-La antibodies, periodic echocardiographic monitoring for the development of isoimmune heart block and isoimmune fetal cardiomyopathy is reasonable.	406
2b	B-NR	7. In anti-Ro-positive pregnancies complicated by fetal heart block, the utilization of fluorinated steroids may be reasonable after shared decision-making discussions as the benefit is uncertain.	402,408
2b	C-LD	8. In pregnancies complicated by fetal heart block secondary to maternal isoimmune disease with fetal cardiomyopathy or hydrops, maternal administration of combined therapy of fluorinated steroids and IVIG therapy may be considered after shared decision-making discussions.	403,404,409,410
3: No benefit	C-LD	9. In pregnancies complicated by fetal bradycardia with a fetal heart rate <55 bpm, the benefit of antenatal maternal administration of beta-adrenergic medications is uncertain, as it has not been shown to improve fetal outcomes and could potentially lead to maternal complications.	403,405

Synopsis

The etiologies of fetal bradycardia (defined as fetal heart rate <110 bpm or less than the third percentile corrected for gestational age) encompass several different mechanisms including SHD, conduction system disturbances manifesting as variable degrees of heart block, and IAS. (Figure 17 outlines the diagnosis and management of fetal bradycardia.) In fetuses with bradycardia, serial sonographic monitoring of fetal status is crucial to identify and treat the development of cardiomyopathy and/or fetal hydrops. Autoimmune-induced heart block and cardiomyopathy may be amenable to antenatal interventions such as maternal steroid administration. However, the benefit of this therapy is uncertain, and its use requires patient-specific shared decision-making between the patient and the cardio-obstetrics team. Pregnancies with idiopathic fetal bradycardia may suggest an IAS, and prenatal and postnatal evaluation to diagnose or rule out IAS is warranted.

Recommendation-specific supportive text

1. While maternal antibody levels can fluctuate, when anti-Ro and anti-La antibodies are present in pregnancies complicated by autoimmune or rheumatologic conditions, fetuses are at risk for the development of cardiac complications, such as isoimmune heart block, hydrops, and cardiomyopathy, including endocardial fibroelastosis independent of conduction system involvement. Pregnancies with prior history of fetal/neonatal isoimmune cardiac disease have at least a 10% risk of recurrence.[411]

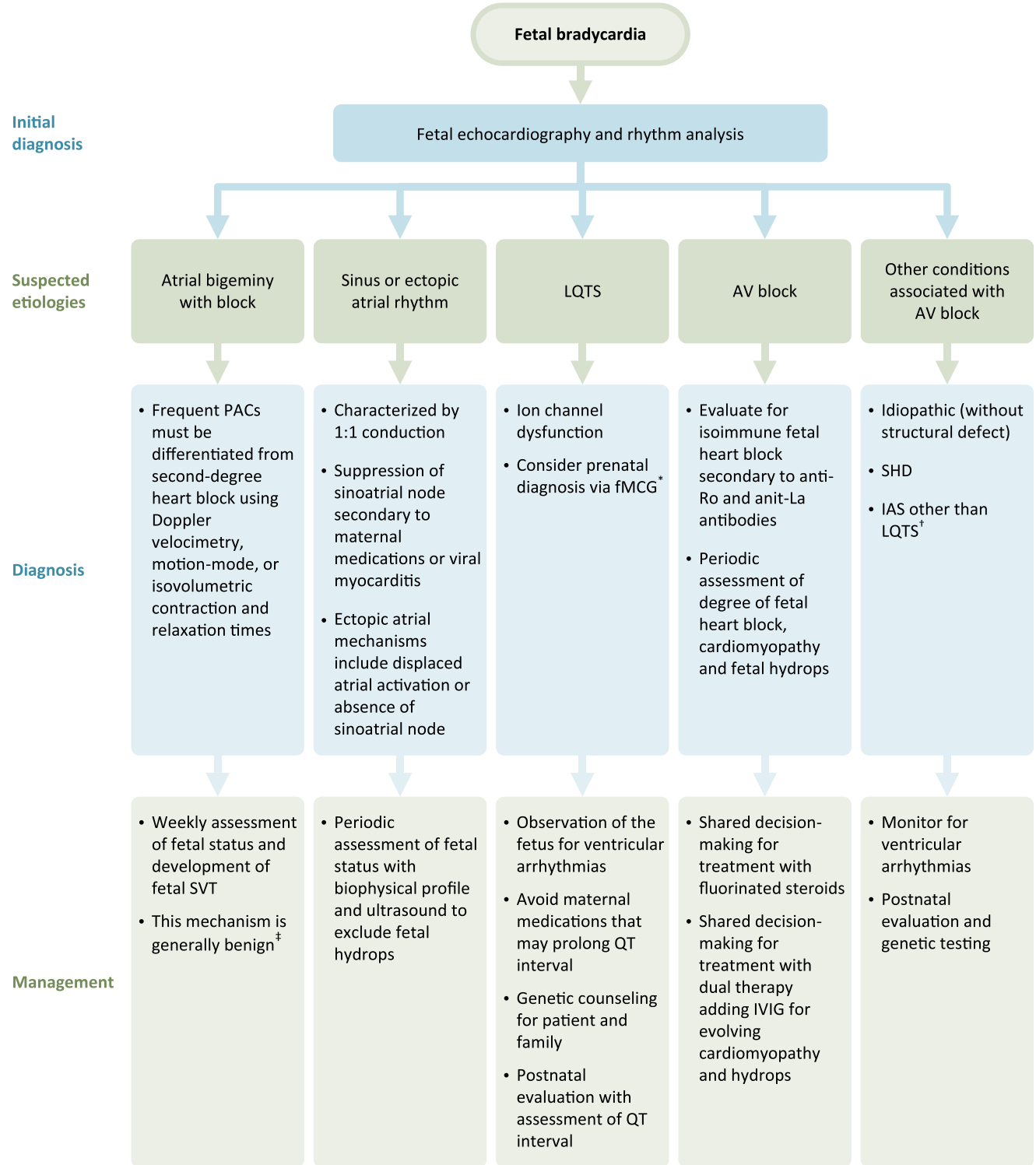

Figure 17 Diagnosis and management of fetal bradycardia. *Hamada et al.[414] †Ishikawa et al.[421] ‡Friedman et al.[422] AV = atrioventricular, fMCG = fetal magnetocardiography, IAS = inherited arrhythmia syndromes, IVIG = intravenous immunoglobulin, LQTS = long QT syndrome, PAC = premature atrial contraction, SHD = structural heart disease.

2. Regardless of etiology, third-degree heart block can lead to fetal hydrops and fetal heart failure, depending upon gestational age. Management includes administration of steroids for fetal lung maturity since fetal deterioration should prompt consideration of premature delivery. Frequent assessment via biophysical profile testing is important in these cases to monitor fetal status.[412]
3. Fetal echocardiogram to evaluate fetal bradycardia may reveal structural cardiac disease, such as corrected

transposition, Ebstein's anomaly, or left atrial isomerism. Detailed use of doppler velocimetry and motion-mode analysis may differentiate second-degree heart block from atrial bigeminy resulting from frequent blocked premature atrial beats. Echocardiography may also reveal cardiomyopathy and heart failure that may evolve in the setting of autoimmune-mediated heart block.[395]

4. The presence of fetal bradycardia may suggest an underlying diagnosis of IAS.[413] Options for prenatal diagnosis are limited, but magnetocardiography, if available, can provide diagnostic confirmation.[414] Prenatal evaluation also includes monitoring fetuses for ventricular arrhythmias. Postnatal evaluation with assessment of neonatal QT interval and mutational ion panels can confirm the diagnosis of suspected IAS. Recommendations for the management of IAS during pregnancy are provided in Section 12.
5. Since the fetal cardiovascular system has an immature Starling capability, fetal cardiac output is rate dependent.[415] Nonstress testing may be unreliable for assessing fetal status in the setting of fetal bradycardia because of blunted autonomic response, which impairs the normal variability of fetal heart patterns generally observed in otherwise healthy fetuses.[416] A normal biophysical profile correlates with reassuring fetal oxygenation and acid/base status.
6. Autoimmune heart block and cardiomyopathy can evolve over a variable period of time and have been reported to occur between weekly fetal assessments.[417] Periodic monitoring to detect evolving disease enables shared decision-making between the patient and her cardio-obstetrics team regarding interventions such as maternal steroid initiation. Additionally, depending upon the gestational age, steroids for fetal lung maturity can be given if further fetal deterioration prompts consideration of preterm birth.
7. The literature demonstrates variables results in the efficacy of antenatal fluorinated steroids for the treatment of fetal heart block. Current literature reporting on steroid treatment for isoimmune heart block is nonrandomized and underpowered. While third-degree heart block has not been demonstrated to be reversible, at least 1 study demonstrates that mild forms of fetal heart block may be reversible.[402] Chronic use of high-dose fluorinated steroids antenatally can lead to potential fetal complications including growth restriction and oligohydramnios. Detailed discussions between the patient and the cardio-obstetrics team are required to weigh potential risks and benefits.
8. Treatment of maternal autoantibody-mediated fetal cardiomyopathy/endocardial fibroelastosis with dual therapy including fluorinated steroids and IVIG may improve outcomes.[404] However, data are limited regarding timing, dosage, and frequency of treatment, and IVIG can cause maternal complications, including infection and hypersensitivity reactions, leading to premature delivery.
9. While beta-adrenergic agents can increase the heart rate in fetuses with fetal bradycardia, overall fetal outcome improvement has not been documented in the literature.[418] Chronic maternal administration of beta-adrenergic agents can lead to severe maternal complications, including pulmonary edema, electrolyte abnormalities, and maternal cardiac dysfunction.[419,420]

Section 12 Inherited arrhythmia syndromes

12.1. Management and risk stratification of inherited arrhythmia syndromes during pregnancy

Inherited arrhythmias syndromes (IAS) encompass a number of conditions, namely LQTS, Brugada syndrome (BrS), CPVT, early repolarization syndrome, Andersen-Tawil syndrome, and short QT syndrome (SQTS). Whether or not a genotype is identified, the vast majority are inherited in an autosomal dominant manner. To date, although genetic testing is exceptionally useful in confirming a clinical diagnosis and providing the opportunity for testing at-risk relatives, it is not universally diagnostic. As such, some individuals will have this diagnosis made clinically with no accompanying pathogenic variant identified. This is particularly the case for BrS, for which there is currently interest in whether the monogenic approach has limited the understanding of this condition, and advice to treat exists regardless of the results of genotyping availability.[15] All of these conditions carry an increased risk for ventricular arrhythmias and sudden cardiac death. They often share the unusual features of being sensitive to precipitants, such as medications or particular environmental situations. Patient education is exceptionally important in these conditions, as affected individuals must learn to modulate their risk. Though many data center on genotype- and phenotype-positive individuals, in some conditions the advice to treat exists regardless of genotyping availability or results.

Management of the pregnant woman with an inherited arrhythmia has a limited evidence base. In the absence of pregnancy-specific data, management is guided by evidence-based treatment established in nonpregnant patients. For the management of the fetus in pregnancies complicated by IAS, specifically LQTS, see Section 12.2.

12.1.1. General management considerations for inherited arrhythmia syndromes in pregnancy

Recommendations for the general management considerations for inherited arrhythmia syndromes in pregnancy			
COR	LOE	Recommendations	References
1	B-NR	1. For pregnancies in families with IAS, genetic testing of the proband is recommended, if not previously performed, for antenatal risk stratification and for optimal management of the fetus and, if affected, the pregnant patient.	153,154
1	B-NR	2. Pregnancies in families with IAS should be evaluated and, preferably, managed by a specialized cardio-obstetrics team with expertise in IAS.	153
1	B-NR	3. In a pregnant patient with an IAS and presumed cardiac syncope or documented VT, referral to an electrophysiologist is recommended for consideration of additional therapeutic interventions, including escalation of pharmacological therapy and possible ICD implantation.	269,423-425
1	C-LD	4. For women and their partners with a documented IAS or who are at risk of an IAS, preconception genetic counseling is recommended, ideally by a trained genetic counselor with expertise in IAS.	153,426
1	C-LD	5. A pregnant patient who survives cardiac arrest due to an IAS should undergo ICD implantation, if indicated, as in the nonpregnant patient.	269,427,428
1	C-EO	6. In pregnant patients with IAS, arrhythmia management should include a review of medications and anesthetic agents for safety, the correction of electrolyte abnormalities, and discussion of situational precipitants.	
1	C-EO	7. Pregnant patients with IAS should have a delivery plan formulated by a cardio-obstetrics team in conjunction with an electrophysiologist or a cardiologist with expertise in arrhythmias during pregnancy, which may include continuous ECG monitoring in accordance with the level of risk and delivery at a facility capable of ACLS for pregnancy.	

Synopsis

In general, women with IAS should continue to be treated throughout pregnancy and in the postpartum period as indicated by their underlying diagnosis. This includes both pharmacological and device therapy, if and as required. Although there are only a small number of case reports of ICD implantation during pregnancy, if an indication arises, ICD implantation is supported by a broader literature showing safety of an existing ICD in pregnancy. As the majority of cases of IAS are autosomal dominant, advice regarding in utero fetal screening for arrhythmias is pertinent regardless of which parent has the diagnosis. Monitoring for in utero fetal growth restriction is necessary during pregnancies in which beta-blockers are used. Delivery and the postpartum period are times of increased arrhythmia risk. Parental education, electrolyte replacement, the arrhythmic potential of medications, and the sympathetic drive of labor are all important considerations. Delivery and postpartum care in a location with cardiac monitoring and prompt life support, including defibrillation, are important because of the increased arrhythmic risk of IAS. An algorithm of recommendations for the general management of IAS during pregnancy is shown in Figure 18. Figure 19 shows the level of surveillance and management of IAS, based on risk during labor and delivery.

Recommendation-specific supportive text

1. Genetic testing results can predict severity of presentation, influence choice of antiarrhythmic drugs, and assist risk stratification for an affected fetus, as well as the pregnant patient, if affected.[429-432] The risk of stillbirth and the incidence of fetal and neonatal life-threatening IAS-related rhythms vary with genotype; for *SCN5A*, phenotypic expression in the fetus and neonate can vary widely.[77,79,153,154,407,429,430,433-438] Of women with prior unexplained stillbirth, 5-10% may have fetuses with IAS.[439,440]
2. Trained multidisciplinary cardio-obstetrics teams reduce mortality and provide consistency of care in high-risk conditions.[25,79,154,429,436] Recently, Cuneo et al,[153] examining 148 pregnancies retrospectively, found that pregnant patients with IAS had an 8-fold higher fetal stillbirth rate and a 2-fold higher miscarriage rate compared with the normal population. This was more

prevalent when the mother had LQTS than when the father had LQTS. The study's main limitation was that only 10% of the fetal deaths underwent genetic testing postmortem, and the mechanism of death remained uncertain; nonetheless, the study indicates a necessity for increased surveillance for fetal well-being. Cardio-obstetrics teams can provide increased surveillance in these cases. The role of nurses and genetic counselors on these teams is critical to provide support for these families. The fetus can be assessed by the cardio-obstetrics team for need for intrauterine transplacental therapy and postnatal treatments, such as antiarrhythmic drugs, pacemakers, and defibrillators.

3. Women with an IAS who experience a syncopal event during pregnancy are better served when evaluated by a cardiac electrophysiologist, if available, or a cardiologist with experience managing pregnant patients. While documentation of a ventricular arrhythmia during the syncopal event greatly assists decision-making, it is recognized that syncope is common in even normal pregnancies; thus, in the absence of arrhythmia documentation, an experienced assessment of the syncopal event can better inform the likely nature of the syncope. It is important to distinguish between common benign causes of syncope, such as vasovagal events, and more concerning syncope deemed to be of cardiac origin (eg, sudden loss of consciousness without a prodrome or clear precipitant). Consideration of alternative medical or therapeutic interventions, according to the underlying diagnosis (eg, addition of an antiarrhythmic agent, left cardiac sympathetic denervation, or an ICD), depends on the clinical scenario and the presumed etiology of the syncope event.[24,27] There are no published cases of left cardiac sympathetic denervation during pregnancy for an IAS, although a single case report details chemical sympathectomy for ischemic VF.[441]
4. The majority of IAS are due to LQTS, of which genotypes LQT1, LQT2, and LQT3 account for about 75-85% of fetal presentations.[25,154,407,429,438] These are primarily of autosomal dominant inheritance with 50% transmission from parent to fetus. In addition, double mutations can occur, especially for the *SCN5A* (LQT3) defects.[407,430,434,437] Preconception genetic counseling is recommended for families affected by IAS to provide all options available to them and offer education to optimize fetal/maternal well-being (such as access to CPR/automated external defibrillator training, support groups, nutritional optimization, medication avoidance, and postnatal genetic testing).[25,79,429,442] Ideally, counseling is provided by a trained genetic counselor or, if unavailable, other providers with expertise in genetics, and includes topics such as risks associated with condition, mode of inheritance, therapy options, and risk to the fetus. An important consideration is the higher risk of miscarriage and fetal death in IAS pregnancies.[153]
5. Decision-making regarding a secondary-prevention ICD in a pregnant woman with an IAS is guided by the standard of care according to the underlying cardiovascular disorder, without regard to the pregnancy status. ICD implantation has been shown to be generally safe during pregnancy with negligible risk from radiation exposure (see Section 4.2). Device implantation after the first trimester is ideal but not essential, since the safety of the pregnant patient is the priority. Pregnancy subsequent to ICD insertion is more frequently described and well-tolerated, and is the preferred clinical pathway if feasible.[269]
6. The usual advice regarding avoidance of arrhythmia precipitants remains significant in pregnancy. This includes the need to consider syndrome-specific drug safety, utilizing www.crediblemeds.org for LQTS, and www.brugadadrugs.org for BrS, checking for electrolyte abnormalities and avoiding situational triggers.[69] As some commonly used drugs found on anesthetic carts and standard labor and delivery protocols are contraindicated in certain IAS, active consideration of drug choice is needed during administration of anesthesia and management of peripartum emergencies.[69]
7. There is a potential for arrhythmic risk during delivery, given the associated sympathetic drive, in women with IAS. A birth plan should be actively formulated, ideally with input from the treating cardiologist and/or electrophysiologist and cardio-obstetrics team. In particular, details need to be specified regarding continuation of medical therapy, location of delivery, type and frequency of monitoring (including whether monitoring needs be continuous), on-demand or stipulated analgesic options (eg, for regional anesthesia to reduce pain and sympathetic drive), vaginal or planned cesarean delivery, and location and duration of postpartum maternal monitoring. For women with an ICD, the location of delivery and duration of postpartum monitoring can potentially be altered; however, no evidence guiding decision-making exists on the optimal delivery location and monitoring duration in this population, and care should be individualized for each clinical situation.

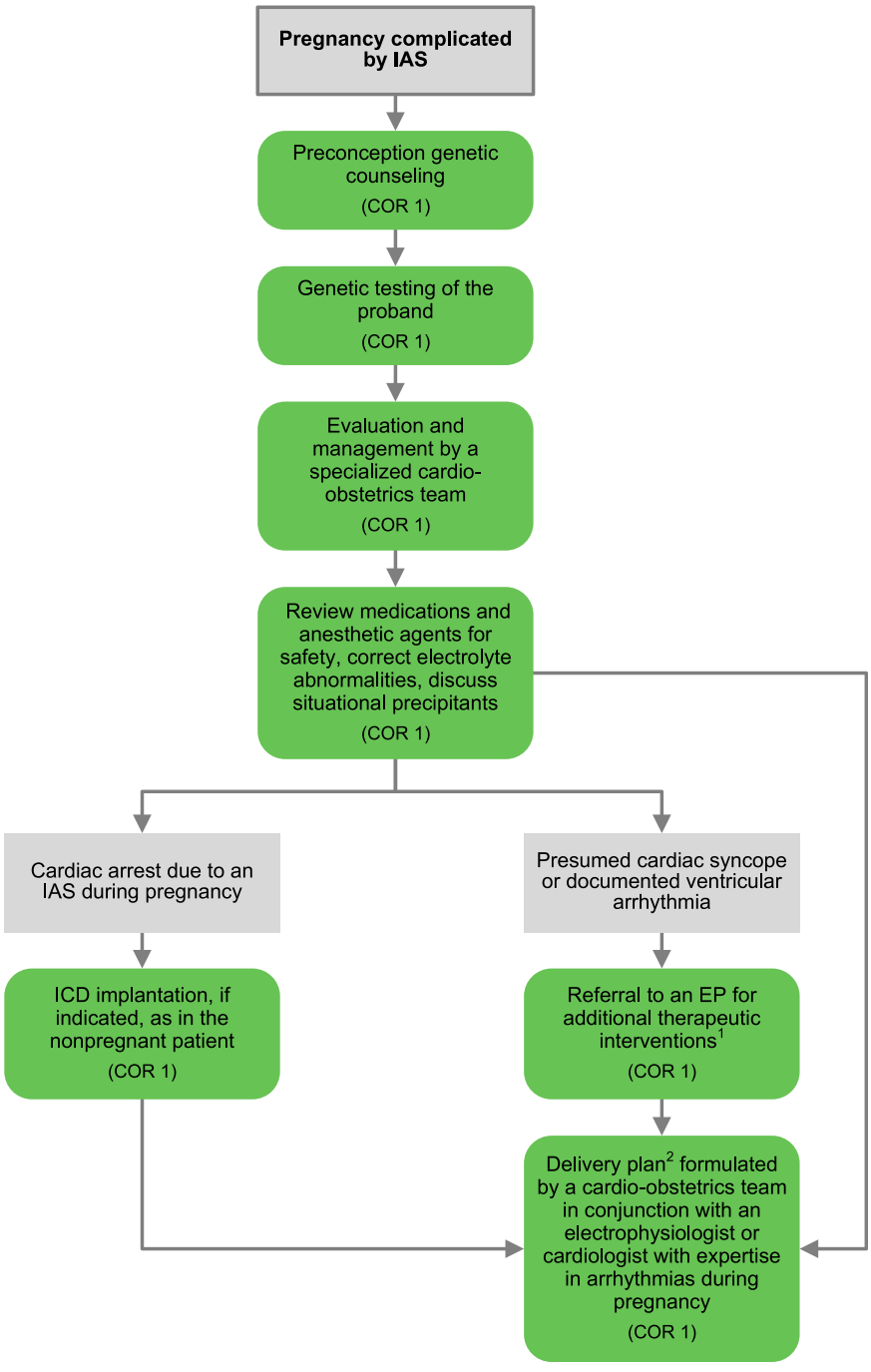

Figure 18 Algorithm for the evaluation and management of pregnancies complicated by inherited arrhythmia syndromes (IAS). Colors correspond to class of recommendation (COR) in Table 1. [1]Therapeutic interventions include escalation of pharmacological therapy and possible implantable cardioverter defibrillator (ICD) implantation. [2]Delivery plan may include continuous electrocardiogram monitoring in accordance with the level of risk and delivery at a facility capable of advanced cardiac life support for pregnancy. EP = electrophysiologist.

Risk for Arrhythmia with Hemodynamic Compromise at Labor & Delivery	Inherited Arrhythmia Syndrome Phenotype	Level of Surveillance
Low-risk	• BrS with no previous events • LQTS with no previous events and QTc ≤470 • Gene-positive CPVT without any phenotype	1
Medium-risk	• BrS and LQTS with remote events • LQTS with no previous events and QTc >470 • CPVT with no recent events and only isolated PVCs on recent EST • ACM with no recent events or NSVT • IVF, SQTS & ERS with no recent events	2
High-risk	• CPVT with recent events and/or recent EST with bigeminal PVCs or higher grade arrhythmia • ACM with recent events and/or NSVT • Any other inherited arrhythmia syndrome with recent events	3

Actions to be Planned for Onset of Labor and Delivery	Surveillance		
	1	2	3
Involvement of a cardio-obstetrics team with expertise in inherited arrhythmia syndromes	X	X	X
Awareness of contra-indicated drugs in the setting of select channelopathies	X	X	X
Continuous telemetry monitoring			X
Intravenous Line		X	X
Preparation of intravenous beta-blocker or anti-arrhythmic drug on unit		X	X
External cardioverter defibrillator on unit		X	X
Arterial line			X

Figure 19 Level of surveillance and management of inherited arrhythmia syndromes based on risk during labor and delivery. Recent events are defined as arrhythmic syncope/seizures, cardiac arrest, and/or sustained ventricular arrhythmia in the preceding 1 year on appropriate therapy. Intravenous line is discretionary for medium-risk situations. ACM = arrhythmogenic cardiomyopathy, BrS = Brugada syndrome, CPVT = catecholaminergic polymorphic ventricular tachycardia, ERS = early repolarization syndrome, EST = exercise stress test, IVF = idiopathic ventricular fibrillation, LQTS = long QT syndrome, NSVT = nonsustained ventricular tachycardia, PVC = premature ventricular contraction, QTc = corrected QT interval, SQTS = short QT syndrome. Adapted with permission from Roston et al.[69]

12.1.2. Management of long QT syndrome in pregnancy

The most common types of the IAS LQTS are LQTS1, LQTS2, and LQTS3, caused by mutations in *KCNQ1*, *KCNH2*, and *SCN5A*, respectively. LQTS carries a risk of TdP, a form of polymorphic VT, which can manifest clinically as syncope or VF causing cardiac arrest and sudden cardiac death.[27] High-risk features for adverse events include a corrected QT interval (QTc) >500 ms and a personal history of prior cardiac events. A gene–sex interaction appears to exist, particularly for women with LQTS2 postpuberty.[443]

Recommendations for management of long QT syndrome in pregnancy

COR	LOE	Recommendations	References
1	B-NR	**1. In pregnant patients with LQTS and a preconception indication for beta-blocker therapy, beta-blockers should be continued throughout pregnancy, delivery, and the postpartum period, including breastfeeding.**	423,444-448
1	B-NR	**2. In pregnant patients with LQTS2, therapy with a beta-blocker, particularly nadolol or propranolol, is recommended particularly during the postpartum period, which represents a high-risk period for cardiac events.**	423,445,448
1	C-LD	**3. In pregnant patients with LQTS who experience cardiac arrest in pregnancy or in whom cardiac syncope or ventricular arrhythmias occur despite beta-blocker use, intensification of therapy including ICD implantation, if indicated, is recommended as in the nonpregnant patient.**	448
1	C-LD	**4. In pregnancies in which either of the parents carry a diagnosis of LQTS, fetal echocardiography is recommended to detect channelopathy-related rhythm abnormalities.**	449
2a	B-NR	**5. In pregnant patients with LQTS who are genotype-positive but phenotype-negative, it is reasonable to treat with a beta-blocker, particularly nadolol or propranolol, after a shared decision-making discussion with the affected woman.**	423,444,448

Synopsis

Preconception counseling of women with LQTS affords an opportunity to repeat risk assessment,[450] including discussion of the potential risks and benefits of beta-blocker use. Retrospective studies have shown that the first cardiac event may occur in pregnancy. The postpartum period is a particularly high-risk time, especially for women with LQTS2 (Figure 20).[423] Long-acting beta-blockers are preferred in LQTS,[15,27] with recent evidence regarding the superiority of nadolol particularly.[450] Although nadolol is generally not recommended during breastfeeding due to relatively high excretion into breast milk,[451] a recent review has suggested it be continued during breastfeeding if it affords rhythm stability in pregnancy.[69] In women with LQTS and an ICD, concomitant beta-blocker therapy is often used to reduce the risk of a cardiac event, including an ICD shock, and, in this circumstance, therapy should be continued during pregnancy.

The general advice regarding avoidance of electrolyte abnormalities, QT-prolonging drugs, and situational triggers that is given to all individuals with this diagnosis (Table 6 and Section 4.3, Recommendation 3) holds true throughout pregnancy and the postpartum period. Additionally, this advice extends to genotype-positive, phenotype-negative (asymptomatic) individuals.[15] This advice is also true for a genotype-negative mother in whom the fetus has inherited an LQTS genotype paternally.[25] As for other types of IAS, labor, delivery, and postpartum monitoring for pregnancies complicated by LQTS should be actively planned and managed (Figure 19 and Section 12.1.1, Recommendation 7).

Recommendation-specific supportive text

1. A number of retrospective studies have shown reduced events in women with LQTS who are treated with beta-blockers during pregnancy and the postpartum period.[423,444-446] Although these are not randomized, the demonstration of serious adverse events in these studies, including cardiac arrest and death, highlights the risk for both mother and fetus/baby. Guidelines recommend longer-acting beta-blockers (eg, nadolol and sustained-release propranolol).[15,24,27,69] Data are insufficient regarding the comparative benefits of different beta-blockers for pregnant patients; therefore, extrapolation from studies in the general LQTS patient population is necessary.[24]
2. Women with LQTS2 are the highest-risk subgroup with this condition in pregnancy and, particularly, the postpartum period. Data strongly support continuation of beta-blocker postdelivery, particularly for the first 9 months postpartum, a period associated with increased risk. The *2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death*[15] suggests that women with LQTS2 with a QTc >500 ms are at particularly high risk and may be candidates for an ICD or a wearable cardioverter defibrillator in the postpartum period.[450] Yet, data on wearable cardioverter defibrillators are scant; to date only a single woman with a wearable cardioverter defibrillator prescribed postpartum could be identified in the literature, and that woman was genotype LQTS1.[452]
3. In pregnant patients with LQTS, serious adverse events, such as cardiac arrest and death, pose greater risk for both mother and fetus/baby than do potential adverse effects from medical therapies. ICDs have been shown to be safe in pregnancy[269] and can be implanted safely with negligible risk from radiation exposure. Defibrillation therapy has also been shown to be well tolerated. In instances when ICD implantation is not feasible, a wearable cardioverter defibrillator is an available option, although data on its use during pregnancy are scant.
4. A fetus with a parent that has a diagnosis of an IAS is at 50% risk of inheriting the same genotype. Fetal echocardiography, including an assessment of the fetal heart rate and rhythm, may help detect ion channelopathy–related rhythm abnormalities, including bradycardia, second-degree heart block, and TdP, all of which can be manifestations of LQTS. Fetal echocardiography is usually performed at around 20 to 22 weeks' gestation, although rhythm disorders are more reliably diagnosed after 27 weeks' gestation.
5. It is reasonable to consider the prescription of beta-blocker to all, including women who are genotype-positive and phenotype-negative (ie, with a normal QTc duration). Identifying the LQTS genotype assists with risk stratification.[450,453,454] Goldenberg et al[453] reported that the cumulative probability of aborted cardiac arrest or sudden cardiac death in patients with LQTS with normal-range QTc intervals (4%) was significantly lower than in those with prolonged QTc intervals (15%) ($P < 0.001$) but higher than in unaffected family members (0.4%). In general terms, women with LQTS2, and all with LQTS2 and LQTS3, appear to be at higher risk than those with LQTS1.[15,455] Decision-making should include a cardiologist, ideally an electrophysiologist, and an obstetrician, as well as the patient.

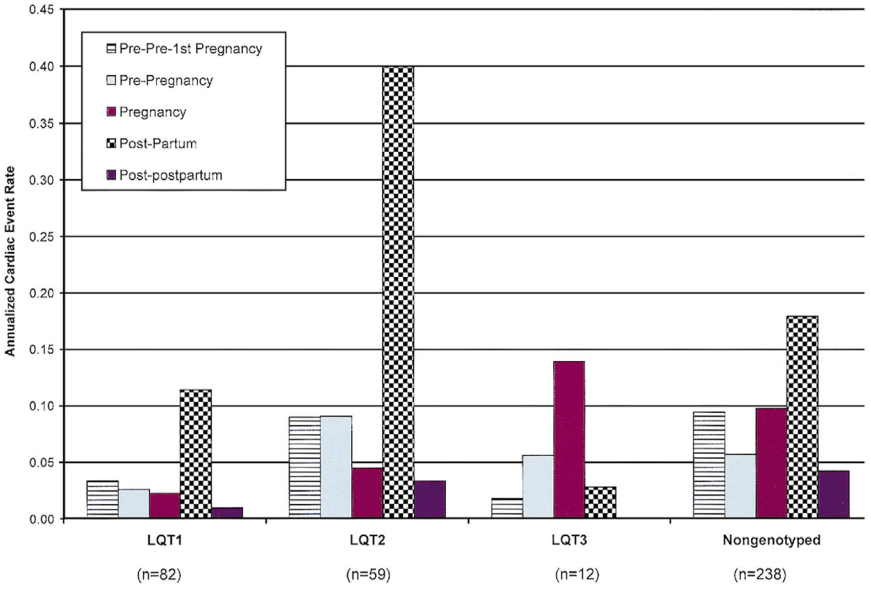

Figure 20 Cardiac event rate according to long QT syndrome (LQTS) genotype and pregnancy status. Reprinted with permission from Seth et al.[423]

12.1.3. Management of Brugada syndrome in pregnancy

Recommendations for management of Brugada syndrome in pregnancy			
COR	LOE	Recommendations	References
1	C-LD	**1. Pregnant and postpartum patients with BrS should be provided with care as in the nonpregnant patient, including continuing therapies for sudden death prevention and avoidance of contraindicated drugs throughout pregnancy and lactation.**	[424]
1	C-LD	**2. In pregnant and postpartum breastfeeding patients with BrS, education about the prompt treatment of fever, such as in cases of mastitis, with antipyretics is recommended, as fever is a potential precipitant for sudden death.**	[456,457]

Synopsis

BrS is an inherited arrhythmia that carries a risk for VF and sudden cardiac death. Fever is a recognized precipitant for arrhythmia in this condition.[458] Although male gender and a spontaneous type 1 BrS–pattern ECG convey an increased risk for events, risk prognostication in this condition remains challenging. In general, women are understood to be at lower risk than men, and pregnancy does not seem to increase risk. Complicating risk prognostication in women, however, are data from meta-analyses suggesting that neither the relationship between a spontaneous type 1 BrS–pattern ECG nor symptom status and future risk in women is helpful.[459,460] Yet, women with this diagnosis should continue to follow general management advice for BrS throughout pregnancy and the postpartum period, namely, treating fever aggressively and avoiding large carbohydrate meals and excess alcohol.[461] It is important to check all medications prescribed in pregnancy, labor, and delivery (www.brugadadrugs.org) and avoid those of concern.

Recommendation-specific supportive text

1. The currently available data on BrS and pregnancy are limited to a single-center retrospective series and a small number of single-case reports. This has been deemed insufficient evidence on which to conclude whether pregnancy is a risk factor for VF and sudden cardiac death in BrS. However, in a report that included 104 women, the risk of arrhythmia did not seem to increase during pregnancy or the postpartum period.[424,462] Care is generally continued during the pregnancy and lactation as in nonpregnant patients, with the avoidance of contraindicated drugs (www.brugadadrugs.org).
2. Fever is known to induce cardiac events in patients with BrS.[456] Given the risk that fever will be a precipitant for sudden cardiac death in patients with BrS, pregnant and postpartum patients with BrS benefit from education about the signs and symptoms of common infections associated with fever, such as mastitis in breastfeeding patients, emphasizing the prompt treatment of fever with antipyretics.[461] The most widely used antipyretic in pregnancy is acetaminophen.

12.1.4. Management of catecholaminergic polymorphic ventricular tachycardia in pregnancy

Recommendations for management of catecholaminergic polymorphic ventricular tachycardia in pregnancy			
COR	LOE	Recommendations	References
1	C-LD	**1. In pregnant patients with CPVT, pharmacological therapy as in the nonpregnant patient should be continued throughout pregnancy and the postpartum period, including during delivery and breastfeeding.**	[463]
1	C-LD	**2. In pregnant patients with CPVT, with symptoms ongoing despite beta-blocker therapy, such as recurrent syncope, VT, or cardiac arrest, intensification of therapy with either the addition of flecainide and/or a left cardiac sympathetic denervation, and/or an ICD is recommended as in the nonpregnant patient.**	[463]
2a	C-LD	**3. In pregnant patients with CPVT who are genotype-positive and phenotype-negative, use of beta-blockers during pregnancy and postpartum is reasonable.**	[463]

Synopsis

CPVT is an uncommon inherited arrhythmia in which polymorphic VT is classically triggered by an adrenergic stressor.[464] Most individuals with this condition become symptomatic early in life.[465] Cardiac events, including death, have been documented in the follow-up of genotype-positive individuals with previously normal exercise stress tests.[465] This underpins the advice in the literature regarding the use

of beta-blockers in CPVT regardless of phenotypic status.[24,464] Guidelines also recommend the addition of flecainide to beta-blockers for individuals with recurrent syncope or sustained VT.[24] In general, an ICD is the first-line option post–cardiac arrest; however, the capacity for a defibrillator shock to perpetuate a VT storm by further adrenergic stimulation has resulted in significant interest in the combined use of beta-blockers, flecainide, and cardiac sympathectomy as a treatment approach, and needs to be taken into account when programming the device.[438,466] The highly malignant nature of this condition means that recommendations in pregnancy should follow those made for the nonpregnant population.

Recommendation-specific supportive text

1. The quality of evidence regarding CPVT in pregnancy is limited. The largest series, a single retrospective study involving 96 women and 228 pregnancies, did not show an increase in events in women with CPVT during pregnancy or the postpartum period. However, as 80% of women in the study underwent pregnancy prior to their CPVT diagnosis, and the average age at diagnosis was 40 years, this appears likely to have been a lower risk subgroup. Furthermore, the cohort did not include women with a CPVT diagnosis who did not undergo pregnancy or in whom death occurred prior to pregnancy, both of whom may have had a higher risk profile. With that said, cardiac events did not occur at a higher rate during pregnancy and the postpartum period than in the nonpregnant state.[463]
2. CPVT presents a unique management situation in the treatment algorithm of cardiac arrest, as epinephrine is contraindicated.[467] Management of VF in CPVT, after direct current shock, consists of intravenous beta-blockers, flecainide, and anesthesia. This diagnosis needs to be identified early, ideally preconception, as it will influence pregnancy-care decision-making, particularly regarding delivery location and associated support. It is important that the delivery plan includes details regarding early regional anesthesia for a vaginal delivery, continuous ECG monitoring, and awareness of the adrenergic stressor of intubation if required. Ventricular arrhythmias are generally managed with intravenous beta-blockers, and these events should result in an immediate call for assistance from the cardiology team. Cardiac arrest will require defibrillation; however, as this may potentiate repeated life-threatening arrhythmias, early utilization of alternative therapies (ie, general anesthesia, antiarrhythmics) is important. Due to the potential for ICD shocks to be an adrenergic stress that perpetuates life-threatening arrhythmias, ICD programming in CPVT should be optimized to deliver therapy for VF.[455]
3. For women with a CPVT pathogenic variant but in whom exercise testing has not revealed a phenotype, there is no available pregnancy-specific literature to guide management. Pharmacological therapy, as in nonpregnant patients,[24,464] is based on the established low risk of beta-blockers during pregnancy and postpartum.[468]

12.1.5. Management of short QT syndrome in pregnancy

Recommendations for management of short QT syndrome in pregnancy

COR	LOE	Recommendations	References
1	C-EO	**1. In pregnant patients with SQTS, arrhythmia-specific treatment should be administered as in the nonpregnant patient and continued throughout pregnancy and the postpartum period.**	

Synopsis

SQTS is a rare, inherited, and highly lethal arrhythmia condition. Both diagnostic and prognostic criteria remain unclear.[469] Medical therapy evidence is small, but quinidine appears to be the best therapeutic option.[15,27,469] AF is common in SQTS, and, though SQTS is rare during pregnancy, SQTS is a diagnostic possibility if a pregnant woman or fetus develops AF.[470]

Recommendation-specific supportive text

1. There are no reported cases in the literature of pregnancy in patients with SQTS. Therefore, it is not possible to provide any advice beyond the generally available literature in this condition. In general, as in most IAS, the standard therapies should be continued throughout pregnancy since the safety of the mother and fetus takes priority. Furthermore, a number of therapies proven effective for SQTS have been used safely during pregnancy, such as ICD implantation; the drugs used in this syndrome, such as quinidine, have a long record of safety in pregnancy and lactation.[69,468]

12.2. Management of inherited fetal arrhythmias

LQTS is the primary IAS in which the fetus manifests arrhythmias. The management of pregnancies of families with IAS should be evaluated and preferably managed by a specialized cardio-obstetrics team, and fetuses should be thoroughly evaluated and closely monitored, since they

have a 50% chance of inheriting IAS and thus are at risk. Potential manifestations of an IAS in the fetus may include bradyarrhythmias; tachyarrhythmias, such as TdP; hydrops; and even fetal demise. A number of clinical tools, such as echocardiography and fetal magnetocardiography (fMCG), are available for evaluation of IAS in the fetus. When arrhythmias are observed, understanding of transplacental administration of pharmacological therapies is essential, with preference given to drugs with the longest experience and record of apparent safe use during pregnancy.

12.2.1. Management of inherited arrhythmia syndromes in the fetus, specifically long QT syndrome

Fetal IAS is used generally in this section, but LQTS is the primary IAS setting in which the fetus manifests arrhythmias.

Recommendations for management of inherited arrhythmia syndromes in the fetus, specifically long QT syndrome

COR	LOE	Recommendations	References
1	B-NR	1. In pregnancies complicated by suspected or documented IAS-related fetal arrhythmias, complete fetal echocardiography is recommended to better evaluate heart anatomy, ventricular function, and arrhythmia mechanisms.	407,426,435,442,471
1	B-NR	2. Fetuses with arrhythmias potentially suggestive of IAS should be referred to a cardio-obstetrics team with expertise in IAS management.	154,426,430,435, 437,472
1	B-NR	3. In pregnancies complicated by suspected or documented IAS, the fetal heart rate should be assessed initially as a baseline and at each prenatal visit and compared against gestation-specific normative values.	153,407,429,435,471
1	B-NR	4. In fetuses with TdP, a maternal intravenous loading dose of magnesium sulfate followed by continuous infusion should be administered as first-line therapy at all stages of pregnancy before considering urgent delivery.	154,426,430
1	C-LD	5. In pregnancies complicated by suspected or documented maternal or fetal IAS, limiting medications that could potentially lengthen the QTc or trigger arrhythmias in the fetus is recommended.	154,426,434,472
2a	B-NR	6. In pregnancies complicated by suspected or documented fetal IAS, fMCG can be beneficial, if available, to identify affected fetuses and IAS-related repolarization abnormalities, and to better assess the severity of the IAS-related arrhythmias.	154,426,430,431,472
2a	B-NR	7. In fetuses with TdP despite magnesium administration, maternal treatment with lidocaine or with a beta-blocker (preferably propranolol) is reasonable at all stages of pregnancy before considering urgent delivery.	154,426,430
2a	C-LD	8. In fetuses with prenatal and postnatal persistent bradycardia, it is reasonable to obtain a postnatal ECG and referral to a pediatric cardiologist or electrophysiologist for further clinical evaluation and genetic testing as indicated to exclude IAS.	154,435
2a	C-LD	9. In fetuses manifesting arrhythmias associated with exposure to QT-prolonging medications, evaluation for maternal nutritional deficiency or concealed maternal or fetal diseases associated with QT prolongation is reasonable.	154,426,429,435,471
3: Harm	C-LD	10. In fetuses with TdP or polymorphic VT associated with potential or documented LQTS, sotalol, procainamide, and amiodarone should not be administered because they can further lengthen QTc and exacerbate arrhythmias.	154,426,435

Synopsis

Of the fetal IAS, most of the arrhythmic events are observed in the setting of LQTS. Fetuses with arrhythmias potentially suggestive of IAS (such as fetal sinus bradycardia, second-degree AV block, complex tachy-brady rhythms, and/or TdP VT) should be referred to a cardio-obstetrics team with expertise in IAS management. When IAS is suspected, the fetal heart rate should be compared against gestation-specific normative values, since bradycardia is a common disease manifestation. Fetal echocardiography can determine the presence of structural defects or hydrops. fMCG can be beneficial for further assessing the type and severity of IAS-related arrhythmias. For TdP in the fetus, magnesium infusion is first-line therapy, followed by lidocaine and non-cardioselective beta-blocker, such as propranolol. Drugs that prolong the QT should not be used to treat TdP in the fetus. Fetuses with prenatal and postnatal persistent bradycardia in the setting of familial IAS should be observed and potentially also referred to specialized centers for further evaluation and management. An algorithm of recommendations for the management of the fetus in pregnancies complicated by potential or documented IAS is shown in Figure 21.

Recommendation-specific supportive text

1. Fetal echocardiography can determine some features of fetal conduction and, most importantly, can detect structural and functional heart conditions, such as hydrops fetalis, LV dysfunction, cardiomyopathy, LV noncompaction, and structural cardiac defects. Anomalies of structure and function are particularly common in fetuses that present with severe symptoms.[432] Fetal echocardiography is readily available and assesses fetal heart rate and rhythm, isovolumic relaxation time, and whether mechanical alternans is present.[436,473] Bundle branch block can sometimes be inferred from flow patterns in the pulmonary veins and aortic arch.[473,474] Yet 45% of TdP was missed by echocardiography in a recent study by Strand et al,[431] because it was not sustained or rapid, and it mimicked other rhythms, including sinus rhythm.[154,430-432,435]
2. Fetuses with suspected TdP or second-degree AV block should be referred to centers with experience in perinatal management of high-risk pregnancies with IAS. Sudden-onset hydrops fetalis or fetal demise in this setting is often due to TdP. At its worst, TdP can be almost continuous, and is usually fatal in these cases.[430] De novo genetic channelopathy variants often present with much more serious symptoms and arrhythmias, including serious novel rhythms, such as slow monomorphic VT and long-cycle-length TdP.[430-432] For a fetal QTc >600 ms, detected by magnetocardiography, the risk of TdP is extremely high. Labor and delivery preparations might include a scheduled delivery with specialists present, having drugs such as intravenous magnesium on hand, and having a neonatal defibrillator/pacer and resuscitation cart readily available.
3. The most common benign IAS-related fetal rhythm is a relative sinus bradycardia for gestation.[154,407,430,434,435,437] Other more serious IAS-related arrhythmias are discussed below. Persistent sinus bradycardia may be suggestive of an IAS, particularly LQT1, although in general, low atrial rhythm and familial bradycardia syndromes with sinus node dysfunction can also cause persistent fetal sinus bradycardia.[25,79,430,435] Nearly all fetuses with LQT1 and roughly half of those with LQT2 had heart rates below the third percentile for gestation.[407,429,430,435,471] Double mutations or uncharacterized mutations have the lowest fetal sinus rates.[434] It is likely that many more LQTS cases could be detected if fetal heart rates were recorded and if gestation-based fetal heart rate normative graphs were used.[25,79,407,471] The fetal heart rate often declines between the 15th and 20th weeks of gestation.[407,429,430,435] About one-third will have blunted fetal heart rate reactivity, making it difficult to use nonstress testing in later pregnancy for obstetrical surveillance.[407,429,430] Biophysical profile assessment is a good alternative to nonstress testing.
4. Unlike SVT, in which early delivery in the close-to-term fetus with hydrops is the treatment of choice, it is reasonable with TdP to attempt to control the tachycardia in utero at any gestation, because TdP is poorly tolerated in the neonate.[430] First-line treatment for fetal TdP consists of transplacental intravenous magnesium sulfate in the same dosing as used for preterm labor (2-6 g loading, then 1-2 g/h infusion for <48 hours, and at levels lower than 6 mEq/L [Table 5]). Magnesium has shown to be extremely effective acutely.[25,79] Transition to alternative drugs within 48 hours is recommended due to neurologic effects to the fetus. It is best if this is managed under the supervision of an expert in IAS, which is often a pediatric electrophysiologist.
5. The most commonly used drugs cross the placenta, and over 165 drugs are now listed as potentially causing QTc prolongation in the population at large. Further, many drugs, such as sotalol, accumulate over time in the amniotic space at concentrations sometimes 20-fold higher than in the maternal serum, and can be recirculated over time through fetal swallowing. A QTc >600 ms has been reported with exposure to opioids and less frequently antiarrhythmic agents, as well as other medications or illicit drugs that are known to lengthen maternal QTc.[426] It is prudent for women with known risk of LQTS to avoid medications that lengthen QTc (https://crediblemeds.org/); furthermore, even if the pregnant patient does not have an IAS but the father does, the fetus has roughly a 50% risk of having an IAS. Acquired QTc prolongation has only recently come to light, and multiple QT-prolonging drug scenarios are additive, and are seen with treatment of mental health conditions.[440] However, not all QT-prolonging drugs can be avoided, such as oxytocin (Pitocin).
6. fMCG, currently the only method to detect repolarization abnormalities,[25,77,154,430,473] is a safe procedure similar to postnatal ECG; despite its name, fMCG does not produce magnetism (unlike MRI). Because fMCG is over 90% sensitive and specific for identifying QT prolongation due to IAS or de novo IAS, it allows the provider to clearly define rhythms and to risk-stratify the fetus. The fMCG test is unparalleled for detecting IAS-related arrhythmias, including TdP, VT, second-degree AV block (2:1, 3:1, 4:1), QTc >600 ms, and QRS or T-wave alternans, low fetal heart rate variability, AFL, and bundle branch block, in various combinations.[431,432] Using fMCG, life-threatening arrhythmias have been seen in ~14% of fetuses with IAS and in

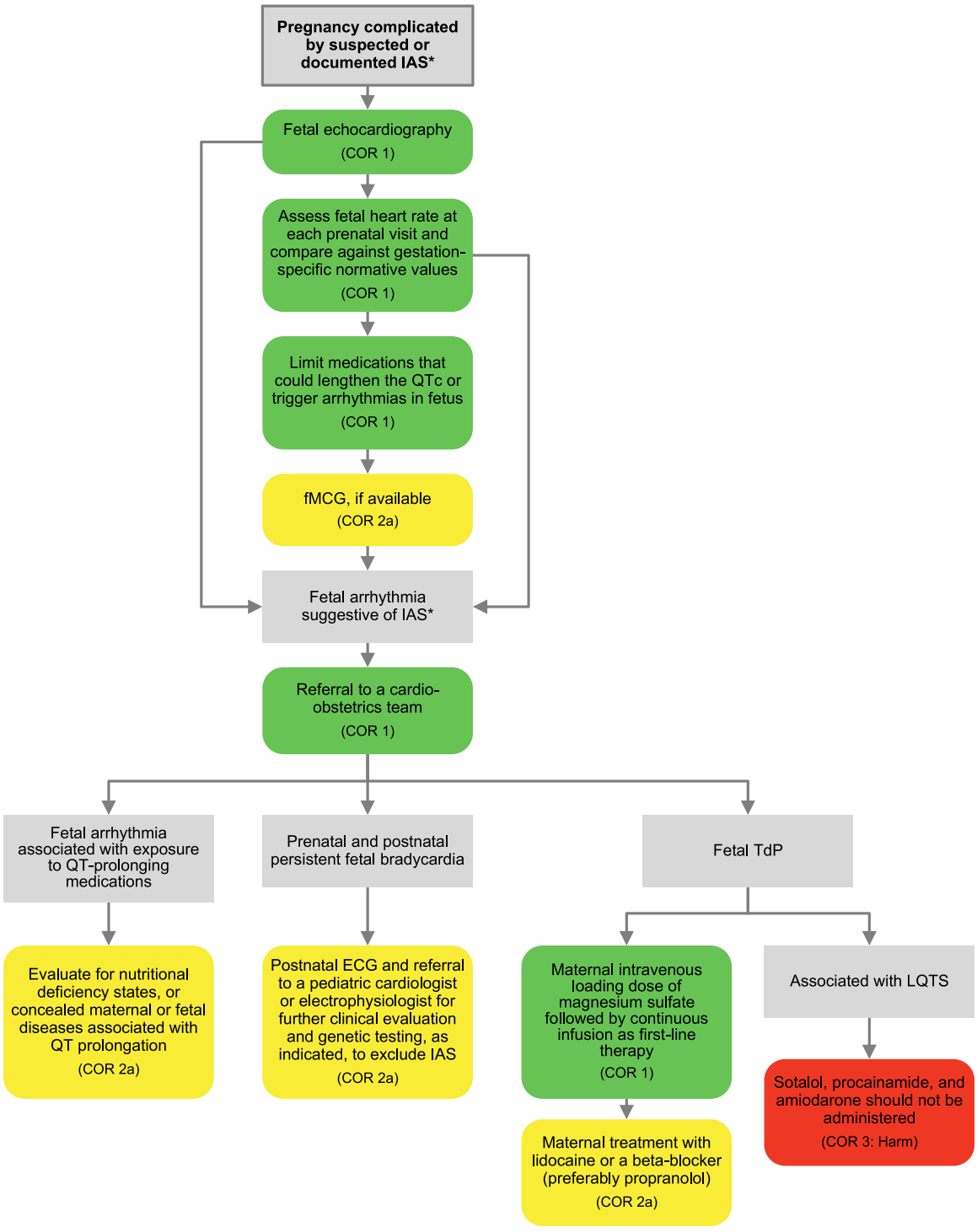

Figure 21 Management of the fetus in pregnancies complicated by potential or documented inherited arrhythmia syndrome (IAS). Colors correspond to the class of recommendation (COR) in Table 1. *Long QT syndrome (LQTS) is the most common IAS setting in which fetuses manifest arrhythmias. ECG = electrocardiogram, fMCG = fetal magnetocardiography, QTc = corrected QT interval, TdP = torsades de pointes.

up to 2/3 of fetuses with de novo arrhythmia syndromes.[407,429,430] In almost all cases, fMCG reduced ambiguity and identified new arrhythmias that had not been suspected based on echocardiography alone, including TdP.[79,430,431,442,473] Although additional sites for fMCG are being established in the United States and Europe, fMCG is currently not widely available. When fMCG is unavailable, fetal echocardiography with weekly obstetric monitoring is an alternative. Fetal ECG, although not FDA-approved, could also be considered, but its efficacy in detecting and characterizing TdP has not been determined.

7. Second-line acute drug treatments for TdP are lidocaine and beta-blockers. Lidocaine (1-1.5 mg/kg intravenous loading, then 1-4 mg/min) can be transitioned to oral mexiletine, but transplacental transfer for mexiletine may not be as consistent. Transplacental transfer of oral propranolol is about 25-40% of the maternal serum concentration.[25,79] There is significant experience with both oral propranolol and metoprolol during pregnancy; however, propranolol may be a preferred option for LQTS. Care must be taken to ensure that short-acting forms are not substituted when sustained release forms are desired and vice versa. Recently, for subjects with poor beta-blocker compliance, nadolol has been used. Labetalol, used frequently for preeclampsia, is not an effective antiarrhythmic treatment, even though its transplacental transfer exceeds that of other beta-blockers. The dosing for these drugs is shown in Table 5.
8. Some IAS manifestations can lead to bradycardia syndromes, such as those caused by *HCN4*, *NKX-2.5*, *KCNJ5*, *SCN5A*, and other IAS. No reports of fetal arrhythmias due to CPVT or type I BrS have been found. There is often quite remarkable overlap between the various manifestations of *SCN5A*, as cardiac conduction disorders and overlap arrhythmias are the most common manifestation regardless of the specific syndromes.[434,437]
9. Opioids, antiarrhythmic drugs, and polypharmacy with multiple QT-prolonging drugs have been associated with excessive QT prolongation (https://www.crediblemeds.org), especially in the presence of electrolyte, mineral, or vitamin D deficiencies. These should be corrected if possible. While therapeutic response is seen in the patient, 25-hydroxy vitamin D levels themselves rarely show a major recovery until after the pregnancy, and thus repeat assessment of levels is not required. Vitamin D serves a critical function of promoting absorption of calcium and magnesium from the gut, and it can be difficult to correct these when 25-hydroxy vitamin D is low.
10. Due to underlying LQTS, antiarrhythmic drugs that lengthen the QTc—especially sotalol, procainamide, and amiodarone—can be proarrhythmic and harmful to the fetus with TdP. In a symptomatic fetus with an *SCN5A* mutation, an alternative option is mexiletine as second-line therapy in conjunction with a beta-blocker.[432] Combination therapies may be considered in situations where delivery is contraindicated and maternal risk is low, and where the parents wish to proceed following counseling on risk. Fetal pacing at this time is not an option.

Section 13 Future directions

Palpitations are one of the most frequent symptoms experienced during pregnancy, and arrhythmias are one of the most frequently encountered cardiac diagnoses. Furthermore, as women are increasingly becoming pregnant later in life and as more women with underlying heart disease survive until childbearing age, the rate of pregnancy-related hospitalizations due to arrhythmias has increased in recent decades. Important gaps in knowledge and areas of uncertainty remain.

An important limitation is the fact that most, if not all, of the data on the management of arrhythmias in pregnancy, for both mother and fetus, are derived from observational studies with small sample sizes. Certainly registries (such as ROPAC) have become important sources of epidemiological knowledge on general risk and outcomes in mother and fetus during pregnancy, as well as the peripartum period, for a number of cardiac conditions.[475] However, registries only collect data on practice patterns already established and as such have limitations. Expanding research by different means, such as creating additional registries, conducting prospective randomized studies, and allocating more funding for research in pregnant populations, is necessary.

The diagnosis and management of patients with an inheritable arrhythmia syndrome require addressing a number of concerns with affected families, such as accuracy and appropriateness of genetic testing, estimated risks for sudden cardiac death, and advising them on transmissibility of the disease to future offspring. Further, implications of genetic testing on future participation in athletics, insurability, and future employment prohibition are important considerations. Thus, a structured approach using a cardiac-genetics team composed of specialized providers, including genetic counselors, would enhance the care and satisfaction of these patients and families; however, those specialized teams and centers remain extremely limited. Thus, increasing the availability of genetic counselors is important.

Sustained fetal arrhythmias may lead to hydrops, cardiac dysfunction, or even stillbirth, and must be recognized and

treated promptly. Recent studies, including some randomized studies on transplacental administration of antiarrhythmic agents, have shed light on pharmacological options in cases of tachyarrhythmia and provide further evidence-based treatment strategies.[108] Yet, the best management of fetuses already affected by hydrops is less clear, and whether direct intrauterine administration of antiarrhythmic drugs or cardiac device therapy should be pursued more aggressively remains uncertain. Also, more widespread use of specialized diagnostic technologies, such as fMCG, could enhance the diagnosis and care of life-threatening arrhythmias in the fetus.

Questions also remain related to optimal positioning of pregnant patients undergoing CPR; these are understandably difficult to answer but could be addressed with studies that use computational modeling, imaging, or registries.

The benefit of anticoagulation in pregnant patients with atrial arrhythmias is uncertain in some populations, unless there is a well-defined high-risk substrate, such as mitral stenosis or a mechanical valve. AF is becoming an increasingly common arrhythmia in pregnancy; however, the decision to administer anticoagulants to these patients is generally based on the CHA_2DS_2VASc score, which has not been validated in pregnant patients.

Lastly, data on drug efficacy, safety, and pharmacokinetics are limited, and, in general, drug choices are driven by anecdotal experience with administration in pregnancy and not necessarily by best option in terms of perceived efficacy for a given arrhythmia. This is because most modern antiarrhythmic drug labels state that drugs have not been properly tested in patients who are pregnant or breastfeeding. Thus, potentially beneficial drugs are frequently deemed dangerous or potentially dangerous in this setting based on the lack of data. One example is dofetilide, a drug that could potentially be used as an alternative to amiodarone in view of the latter's significant side effect profile, yet reports on dofetilide use during pregnancy are essentially nonexistent. Similarly, data on the safety and efficacy of direct oral anticoagulants during pregnancy are lacking. In addition to targeted studies of drugs for use in pregnant patients and fetuses with arrhythmias, inclusion rather than exclusion of pregnant patients in new clinical trials of antiarrhythmic and anticoagulant drugs may be warranted.

Appendix

Supplementary Data

Supplementary data (Appendix 3) associated with this article can be found in the online version at https://doi.org/10.1016/j.hrthm.2023.05.017.

References

1. Indik JH, Patton KK, Beardsall M, et al. HRS clinical document development methodology manual and policies: executive summary. Heart Rhythm 2017;14:e495–e500.
2. Graham R, Mancher M, Miller Wolman D, Greenfield S, Steinberg E. Clinical Practice Guidelines We Can Trust. National Academies Press; 2011.
3. Halperin JL, Levine GN, Al-Khatib SM, et al. Further evolution of the ACC/AHA clinical practice guideline recommendation classification system: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines. J Am Coll Cardiol 2016;67:1572–1574.
4. Steffel J, Collins R, Antz M, et al. 2021 European Heart Rhythm Association practical guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. Europace 2021;23:1612–1676.
5. Hindricks G, Potpara T, Dagres N, et al. 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J 2021;42:373–498.
6. Ommen SR, Mital S, Burke MA, et al. 2020 AHA/ACC guideline for the diagnosis and treatment of patients with hypertrophic cardiomyopathy: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation 2020;142:e558–e631.
7. Mehta LS, Warnes CA, Bradley E, et al. Cardiovascular considerations in caring for pregnant patients: a scientific statement from the American Heart Association. Circulation 2020;141:e884–e903.
8. Brugada J, Katritsis DG, Arbelo E, et al. 2019 ESC guidelines for the management of patients with supraventricular tachycardia The Task Force for the management of patients with supraventricular tachycardia of the European Society of Cardiology (ESC). Eur Heart J 2020;41:655–720.
9. January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Heart Rhythm 2019;16:e66–e93.
10. Towbin JA, McKenna WJ, Abrams DJ, et al. 2019 HRS expert consensus statement on evaluation, risk stratification, and management of arrhythmogenic cardiomyopathy. Heart Rhythm 2019;16:e301–e372.
11. Kusumoto FM, Schoenfeld MH, Barrett C, et al. 2018 ACC/AHA/HRS guideline on the evaluation and management of patients with bradycardia and cardiac conduction delay: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Heart Rhythm 2019;16:e128–e226.
12. Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, et al. 2018 ESC guidelines for the management of cardiovascular diseases during pregnancy. Eur Heart J 2018;39:3165–3241.
13. Brignole M, Moya A, de Lange FJ, et al. 2018 ESC guidelines for the diagnosis and management of syncope. Eur Heart J 2018;39:1883–1948.
14. Dan GA, Martinez-Rubio A, Agewall S, et al. Antiarrhythmic drugs-clinical use and clinical decision making: a consensus document from the European Heart Rhythm Association (EHRA) and European Society of Cardiology (ESC) Working Group on Cardiovascular Pharmacology, endorsed by the Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS) and International Society of Cardiovascular Pharmacotherapy (ISCP). Europace 2018;20:731–732an.
15. Al-Khatib SM, Stevenson WG, Ackerman MJ, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. Heart Rhythm 2018;15:e73–e189.
16. Canobbio MM, Warnes CA, Aboulhosn J, et al. Management of pregnancy in patients with complex congenital heart disease: a scientific statement for healthcare professionals from the American Heart Association. Circulation 2017;135:e50–e87.
17. Katritsis DG, Boriani G, Cosio FG, et al. European Heart Rhythm Association (EHRA) consensus document on the management of supraventricular arrhythmias, endorsed by Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS), and Sociedad Latinoamericana de Estimulacion Cardiaca y Electrofisiologia (SOLAECE). Europace 2017;19:465–511.
18. Shen W-K, Sheldon Robert S, Benditt DG, Cohen MI, et al. 2017 ACC/AHA/HRS guideline for the evaluation and management of patients with syncope: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Heart Rhythm 2017;14:e155–e217.
19. Page RL, Joglar JA, Caldwell MA, et al. 2015 ACC/AHA/HRS guideline for the management of adult patients with supraventricular tachycardia: a report of the American College of Cardiology/American Heart Association Task Force on

Clinical Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2016;67:e27–e115.
20. Zipes DP, Calkins H, Daubert JP, et al. 2015 ACC/AHA/HRS advanced training statement on clinical cardiac electrophysiology (a revision of the ACC/AHA 2006 update of the clinical competence statement on invasive electrophysiology studies, catheter ablation, and cardioversion). Heart Rhythm 2016;13:e3–e37.
21. Jeejeebhoy FM, Zelop CM, Lipman S, et al. Cardiac arrest in pregnancy: a scientific statement from the American Heart Association. Circulation 2015; 132:1747–1773.
22. Kleinman ME, Brennan EE, Goldberger ZD, et al. Part 5: Adult basic life support and cardiopulmonary resuscitation quality: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2015;132:S414–435.
23. Link MS, Berkow LC, Kudenchuk PJ, et al. Part 7: Adult advanced cardiovascular life support: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2015;132:S444–464.
24. Priori SG, Blomstrom-Lundqvist C, Mazzanti A, et al. 2015 ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). Endorsed by Association for European Paediatric and Congenital Cardiology (AEPC). Eur Heart J 2015; 36:2793–2867.
25. Donofrio MT, Moon-Grady AJ, Hornberger LK, et al. Diagnosis and treatment of fetal cardiac disease: a scientific statement from the American Heart Association. Circulation 2014;129:2183–2242.
26. Anderson JL, Halperin JL, Albert NM, et al. Management of patients with atrial fibrillation (compilation of 2006 ACCF/AHA/ESC and 2011 ACCF/AHA/HRS recommendations): a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013;61:1935–1944.
27. Priori SG, Wilde AA, Horie M, et al. HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes: document endorsed by HRS, EHRA, and APHRS in May 2013 and by ACCF, AHA, PACES, and AEPC in June 2013. Heart Rhythm 2013;10:1932–1963.
28. Ackerman MJ, Priori SG, Willems S, et al. HRS/EHRA expert consensus statement on the state of genetic testing for the channelopathies and cardiomyopathies: This document was developed as a partnership between the Heart Rhythm Society (HRS) and the European Heart Rhythm Association (EHRA). Heart Rhythm 2011;8:1308–1339.
29. Douglas PS, Garcia MJ, Haines DE, et al. ACCF/ASE/AHA/ASNC/HFSA/HRS/SCAI/SCCM/SCCT/SCMR 2011 appropriate use criteria for echocardiography: a report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Society of Echocardiography, American Heart Association, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Critical Care Medicine, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance American College of Chest Physicians. J Am Soc Echocardiogr 2011;24:229–267.
30. Davis MB, Walsh MN. Cardio-obstetrics. Circ Cardiovas Qual Outcomes 2019; 12:e005417.
31. ACOG committee opinion no. 579: Definition of term pregnancy. Obstet Gynecol 2013;122:1139–1140.
32. Committee on Obstetric Practice. ACOG committee opinion no. 831: Medically indicated late-preterm and early-term deliveries. Obstet Gynecol 2021; 138:e35–e39.
33. Shotan A, Ostrzega E, Mehra A, Johnson JV, Elkayam U. Incidence of arrhythmias in normal pregnancy and relation to palpitations, dizziness, and syncope. Am J Cardiol 1997;79:1061–1064.
34. Al-Yaseen E, Al-Na'ar A, Hassan M, Al-Ostad G, Ibrahim E. Palpitation in pregnancy: experience in one major hospital in Kuwait. Med J Islam Repub Iran 2013;27:31–34.
35. Choi HS, Han SS, Choi HA, et al. Dyspnea and palpitation during pregnancy. Korean J Intern Med 2001;16:247–249.
36. Sanghavi M, Rutherford JD. Cardiovascular physiology of pregnancy. Circulation 2014;130:1003–1008.
37. Vaidya VR, Arora S, Patel N, et al. Burden of arrhythmia in pregnancy. Circulation 2017;135:619–621.
38. Li JM, Nguyen C, Joglar JA, Hamdan MH, Page RL. Frequency and outcome of arrhythmias complicating admission during pregnancy: experience from a high-volume and ethnically-diverse obstetric service. Clin Cardiol 2008;31:538–541.
39. Salam AMF, Hall R, Johnson MR, et al. Impact of atrial fibrillation/flutter during pregnancy on maternal mortality in patients with heart disease; analysis from the ROPAC registry. Eur Heart 2014;35:574-574.
40. Hameed A, Karaalp IS, Tummala PP, et al. The effect of valvular heart disease on maternal and fetal outcome of pregnancy. J Am Coll Cardiol 2001; 37:893–899.
41. Cruz MO, Hibbard JU, Alexander T, Briller J. Ambulatory arrhythmia monitoring in pregnant patients with palpitations. Am J Perinatol 2013;30:53–58.
42. Sharp A, Patient C, Pickett J, Belham M. Pregnancy-related inappropriate sinus tachycardia: A cohort analysis of maternal and fetal outcomes. Obstet Med 2021;14:230–234.
43. Shabtaie SA, Witt CM, Asirvatham SJ. Natural history and clinical outcomes of inappropriate sinus tachycardia. J Cardiovasc Electrophysiol 2020;31:137–143.
44. Lee SH, Chen SA, Wu TJ, et al. Effects of pregnancy on first onset and symptoms of paroxysmal supraventricular tachycardia. Am J Cardiol 1995; 76:675–678.
45. Silversides CK, Harris L, Haberer K, Sermer M, Colman JM, Siu SC. Recurrence rates of arrhythmias during pregnancy in women with previous tachyarrhythmia and impact on fetal and neonatal outcomes. Am J Cardiol 2006; 97:1206–1212.
46. Silversides CK, Grewal J, Mason J, et al. Pregnancy outcomes in women with heart disease: The CARPREG II Study. J Am Coll Cardiol 2018;71:2419–2430.
47. Chatur S, Islam S, Moore LE, Sandhu RK, Sheldon RS, Kaul P. Incidence of syncope during pregnancy: temporal trends and outcomes. J Am Heart Assoc 2019;8:e011608.
48. Howard BK, Goodson JH, Mengert WF. Supine hypotensive syndrome in late pregnancy. Obstet Gynecol 1953;1:371–377.
49. Holmes F. Incidence of the supine hypotensive syndrome in late pregnancy. A clinical study in 500 subjects. J Obstet Gynaecol Br Emp 1960;67:254–258.
50. Humphries A, Mirjalili SA, Tarr GP, Thompson JMD, Stone P. The effect of supine positioning on maternal hemodynamics during late pregnancy. J Matern Fetal Neonatal Med 2019;32:3923–3930.
51. Higuchi H, Takagi S, Zhang K, Furui I, Ozaki M. Effect of lateral tilt angle on the volume of the abdominal aorta and inferior vena cava in pregnant and nonpregnant women determined by magnetic resonance imaging. Anesthesiology 2015;122:286–293.
52. Rossi A, Cornette J, Johnson MR, et al. Quantitative cardiovascular magnetic resonance in pregnant women: cross-sectional analysis of physiological parameters throughout pregnancy and the impact of the supine position. J Cardiovasc Magn Reson 2011;13:31.
53. Sherer DM, Santoso P, Russell BA, Abulafia O. Micturition syncope during pregnancy. Obstet Gynecol 2005;105:485–486.
54. Wang Y, Joyner RW, Wagner MB, Cheng J, Lai D, Crawford BH. Stretch-activated channel activation promotes early afterdepolarizations in rat ventricular myocytes under oxidative stress. Am J Physiol Heart Circ Physiol 2009; 296:H1227–H1235.
55. Enriquez AD, Economy KE, Tedrow UB. Contemporary management of arrhythmias during pregnancy. Circ Arrhythm Electrophysiol 2014;7:961–967.
56. Barron WM, Mujais SK, Zinaman M, Bravo EL, Lindheimer MD. Plasma catecholamine responses to physiologic stimuli in normal human pregnancy. Am J Obstet Gynecol 1986;154:80–84.
57. Roberts JM, Insel PA, Goldfien A. Regulation of myometrial adrenoreceptors and adrenergic response by sex steroids. Mol Pharmacol 1981;20:52–58.
58. Matsuo H, Inoue K, Hapsari ED, Kitano K, Shiotani H. Change of autonomic nervous activity during pregnancy and its modulation of labor assessed by spectral heart rate variability analysis. Clin Exp Obstet Gynecol 2007;34:73–79.
59. Soma-Pillay P, Nelson-Piercy C, Tolppanen H, Mebazaa A. Physiological changes in pregnancy. Cardiovasc J Afr 2016;27:89–94.
60. Costantine MM. Physiologic and pharmacokinetic changes in pregnancy. Front Pharmacol 2014;5:65.
61. Fitton CA, Steiner MFC, Aucott L, et al. In-utero exposure to antihypertensive medication and neonatal and child health outcomes: a systematic review. J Hypertens 2017;35:2123–2137.
62. Ersboll AS, Hedegaard M, Sondergaard L, Ersboll M, Johansen M. Treatment with oral beta-blockers during pregnancy complicated by maternal heart disease increases the risk of fetal growth restriction. BJOG 2014;121:618–626.
63. Duan L, Ng A, Chen W, Spencer HT, Lee MS. Beta-blocker subtypes and risk of low birth weight in newborns. J Clin Hypertens (Greenwich) 2018; 20:1603–1609.
64. Halpern DG, Weinberg CR, Pinnelas R, Mehta-Lee S, Economy KE, Valente AM. Use of medication for cardiovascular disease during pregnancy: JACC state-of-the-art review. J Am Coll Cardiol 2019;73:457–476.
65. Grewal J, Siu SC, Lee T, et al. Impact of beta-blockers on birth weight in a high-risk cohort of pregnant women with CVD. J Am Coll Cardiol 2020; 75:2751–2752.

66. Devlin RG, Duchin KL, Fleiss PM. Nadolol in human serum and breast milk. Br J Clin Pharmacol 1981;12:393–396.
67. Riant P, Urien S, Albengres E, Duche JC, Tillement JP. High plasma protein binding as a parameter in the selection of betablockers for lactating women. Biochem Pharmacol 1986;35:4579–4581.
68. Taylor C, Stambler BS. Management of long QT syndrome in women before, during, and after pregnancy. US Cardiology Review 2021;15:e08.
69. Roston TM, van der Werf C, Cheung CC, et al. Caring for the pregnant woman with an inherited arrhythmia syndrome. Heart Rhythm 2020;17:341–348.
70. Pernia S, DeMaagd G. The new Pregnancy And Lactation Labeling Rule. P T 2016;41:713–715.
71. U.S. Food and Drug Administration. Content and format of labeling for human prescription drug and biological products; requirements for pregnancy and lactation labeling. Final rule. Fed Regist 2014;79:72063–72103. www.gpo.gov/fdsys/pkg/FR-72014-72012-72004/pdf/72014-28241.pdf.
72. Byrne JJ, Saucedo AM, Spong CY. Evaluation of drug labels following the 2015 Pregnancy and Lactation Labeling Rule. JAMA Network Open 2020;3:e2015094.
73. Simpson JM, Sharland GK. Fetal tachycardias: management and outcome of 127 consecutive cases. Heart 1998;79:576–581.
74. Cuneo BF, Strasburger JF. Management strategy for fetal tachycardia. Obstet Gynecol 2000;96:575–581.
75. Oudijk MA, Ruskamp JM, Ambachtsheer BE, et al. Drug treatment of fetal tachycardias. Paediatr Drugs 2002;4:49–63.
76. Hornberger LK, Sahn DJ. Rhythm abnormalities of the fetus. Heart 2007;93:1294–1300.
77. Strasburger JF, Wakai RT. Fetal cardiac arrhythmia detection and in utero therapy. Nat Rev Cardiol 2010;7:277–290.
78. Jaeggi ET, Carvalho JS, De Groot E, et al. Comparison of transplacental treatment of fetal supraventricular tachyarrhythmias with digoxin, flecainide, and sotalol: results of a nonrandomized multicenter study. Circulation 2011;124:1747–1754.
79. Wacker-Gussmann A, Strasburger JF, Cuneo BF, Wakai RT. Diagnosis and treatment of fetal arrhythmia. Am J Perinatol 2014;31:617–628.
80. Miyoshi T, Maeno Y, Hamasaki T, et al. Antenatal therapy for fetal supraventricular tachyarrhythmias: Multicenter trial. J Am Coll Cardiol 2019;74:874–885.
81. Cuneo BF. Treatment of fetal tachycardia. Heart Rhythm 2008;5:1216–1218.
82. Georgiopoulos G, Tsiachris D, Kordalis A, et al. Pharmacotherapeutic strategies for atrial fibrillation in pregnancy. Expert Opin Pharmacother 2019;20:1625–1636.
83. Gowda RM, Khan IA, Mehta NJ, Vasavada BC, Sacchi TJ. Cardiac arrhythmias in pregnancy: clinical and therapeutic considerations. Int J Cardiol 2003;88:129–133.
84. Ito S. Transplacental treatment of fetal tachycardia: implications of drug transporting proteins in placenta. Semin Perinatol 2001;25:196–201.
85. Joglar JA, Page RL. Antiarrhythmic drugs in pregnancy. Curr Opin Cardiol 2001;16:40–45.
86. Joglar JA, Page RL. Management of arrhythmia syndromes during pregnancy. Curr Opin Cardiol 2014;29:36–44.
87. Maeno Y, Hirose A, Kanbe T, Hori D. Fetal arrhythmia: Prenatal diagnosis and perinatal management. J Obstet Gynaecol Res 2009;35:623–629.
88. Omar HA, Rhodes LA, Ramirez R, Arsich J, Einzig S. Alteration of human placental vascular tone by antiarrhythmic medications in vitro. J Cardiovasc Electrophysiol 1996;7:1197–1203.
89. Page RL, Hamdan MH, Joglar JA. Arrhythmias occurring during pregnancy. Card Electrophysiol Rev 2002;6:136–139.
90. Schmolling J, Renke K, Richter O, Pfeiffer K, Schlebusch H, Holler T. Digoxin, flecainide, and amiodarone transfer across the placenta and the effects of an elevated umbilical venous pressure on the transfer rate. Ther Drug Monit 2000;22:582–588.
91. Schneider H. Drug treatment in pregnancy. Curr Opin Obstet Gynecol 1994;6:50–57.
92. Allen L, Hornberger, Lisa K, Sharland G. Fetal Arrhythmias. Textbook of Fetal Cardiology, Vol 1. Greenwich Medical Media, Limited; 2000:421–452.
93. Srinivasan S, Strasburger J. Overview of fetal arrhythmias. Curr Opin Pediatr 2008;20:522–531.
94. Strasburger JF, Cheulkar B, Wichman HJ. Perinatal arrhythmias: diagnosis and management. Clin Perinatol 2007;34:627–652.
95. Tincani A, Rebaioli CB, Frassi M, et al. Pregnancy and autoimmunity: maternal treatment and maternal disease influence on pregnancy outcome. Autoimmun Rev 2005;4:423–428.
96. Trappe JH. Emergency therapy of maternal and fetal arrhythmias during pregnancy. J Emerg Trauma Shock 2010;3:153–159.
97. Parilla BV, Strasburger JF, Socol ML. Fetal supraventricular tachycardia complicated by hydrops fetalis: a role for direct fetal intramuscular therapy. Am J Perinatol 1996;13:483–486.
98. Carvalho SJ. Fetal dysrhythmias. Best Pract Res Clin Obstet Gynaecol 2019;58:28–41.
99. Malhame I, Gandhi C, Tarabulsi G, et al. Maternal monitoring and safety considerations during antiarrhythmic treatment for fetal supraventricular tachycardia. Obstet Med 2019;12:66–75.
100. Strasburger FJ. Predictability in fetal supraventricular tachycardia management. J Am Coll Cardiol 2019;74:886–888.
101. Burrows K, Fox J, Biblo LA, Roth JA. Pregnancy and short-coupled torsades de pointes. Pacing Clin Electrophysiol 2013;36:e77–79.
102. Kayentao K, Guirou EA, Doumbo OK, et al. Preliminary study of quinine pharmacokinetics in pregnant women with malaria-HIV co-infection. Am J Trop Med Hyg 2014;90:530–534.
103. Wang X, Song Y, Wu D, et al. Inter-individual variations and modulators of MDR1 transport activity in human placenta. Placenta 2020;97:46–50.
104. Betrian Blasco P, Antunez Jimenez MI, Falcon Gonzalez LH, Suarez Cabrera P. Neonatal life-threatening arrhythmia responding to lidocaine, a probable LQTS3. Int J Cardiol 2007;117:e61–e63.
105. Joglar JA, Page RL. Treatment of cardiac arrhythmias during pregnancy: safety considerations. Drug Saf 1999;20:85–94.
106. Mittadodla PS, Salen PN, Traub DM. Isoproterenol as an adjunct for treatment of idiopathic ventricular fibrillation storm in a pregnant woman. Am J Emerg Med 2012;30:e253–e255.
107. Chang CC, Acharfi S, Wu MH, et al. A novel SCN5A mutation manifests as a malignant form of long QT syndrome with perinatal onset of tachycardia/bradycardia. Cardiovasc Res 2004;64:268–278.
108. Alsaied T, Baskar S, Fares M, et al. First-line antiarrhythmic transplacental treatment for fetal tachyarrhythmia: A systematic review and meta-analysis. J Am Heart Assoc 2017;6:e007164.
109. Rasheed A, Simpson J, Rosenthal E. Neonatal ECG changes caused by supratherapeutic flecainide following treatment for fetal supraventricular tachycardia. Heart 2003;89:470.
110. Trotter A, Kaestner M, Pohlandt F, Lang D. Unusual electrocardiogram findings in a preterm infant after fetal tachycardia with hydrops fetalis treated with flecanide. Pediatr Cardiol 2000;21:259–262.
111. Allan LD, Chita SK, Sharland GK, Maxwell D, Priestley K. Flecainide in the treatment of fetal tachycardias. Br Heart J 1991;65:46–48.
112. Capucci A, Boriani G. Propafenone in the treatment of cardiac arrhythmias. A risk-benefit appraisal. Drug Saf 1995;12:55–72.
113. Khan IA, Nair CK, Singh N, Gowda RM, Nair RC. Acute ventricular rate control in atrial fibrillation and atrial flutter. Int J Cardiol 2004;97:7–13.
114. Madonia S, De Simone M, Brai G, et al. Intravenous versus oral initial load of propafenone for conversion of recent-onset atrial fibrillation in the emergency room: a randomized trial. Ital Heart J 2000;1:475–479.
115. Sonesson SE, Fouron JC, Wesslen-Eriksson E, Jaeggi E, Winberg P. Foetal supraventricular tachycardia treated with sotalol. Acta Paediatr 1998;87:584–587.
116. Chockalingam P, Crotti L, Girardengo G, et al. Not all beta-blockers are equal in the management of long QT syndrome types 1 and 2: higher recurrence of events under metoprolol. J Am Coll Cardiol 2012;60:2092–2099.
117. Erkkola R, Lammintausta R, Liukko P, Anttila M. Transfer of propranolol and sotalol across the human placenta. Their effect on maternal and fetal plasma renin activity. Acta Obstet Gynecol Scand 1982;61:31–34.
118. Ito S, Magee L, Smallhorn J. Drug therapy for fetal arrhythmias. Clin Perinatol 1994;21:543–572.
119. Oudijk MA, Stoutenbeek P, Sreeram N, Visser GH, Meijboom EJ. Persistent junctional reciprocating tachycardia in the fetus. J Matern Fetal Neonatal Med 2003;13:191–196.
120. Schneider H, Proegler M. Placental transfer of beta-adrenergic antagonists studied in an in vitro perfusion system of human placental tissue. Am J Obstet Gynecol 1988;159:42–47.
121. Smith MT, Livingstone I, Eadie MJ, Hooper WD, Triggs EJ. Metabolism of propranolol in the human maternal-placental-foetal unit. Eur J Clin Pharmacol 1983;24:727–732.
122. Feely J, Peden N. Use of beta-adrenoceptor blocking drugs in hyperthyroidism. Drugs 1984;27:425–446.
123. Bateman BT, Patorno E, Desai RJ, et al. Late pregnancy ß blocker exposure and risks of neonatal hypoglycemia and bradycardia. Pediatrics 2016;138.
124. van der Heijden LB, Oudijk MA, Manten GT, ter Heide H, Pistorius L, Freund MW. Sotalol as first-line treatment for fetal tachycardia and neonatal follow-up. Ultrasound Obstet Gynecol 2013;42:285–293.

125. Oudijk MA, Ruskamp JM, Ververs FF, et al. Treatment of fetal tachycardia with sotalol: transplacental pharmacokinetics and pharmacodynamics. J Am Coll Cardiol 2003;42:765–770.
126. Bartalena L, Bogazzi F, Braverman LE, Martino E. Effects of amiodarone administration during pregnancy on neonatal thyroid function and subsequent neurodevelopment. J Endocrinol Invest 2001;24:116–130.
127. Jouannic JM, Delahaye S, Fermont L, et al. Fetal supraventricular tachycardia: a role for amiodarone as second-line therapy? Prenat Diagn 2003;23:152–156.
128. Strasburger JF, Cuneo BF, Michon MM, et al. Amiodarone therapy for drug-refractory fetal tachycardia. Circulation 2004;109:375–379.
129. Moatassim S, Touleimat S, Hazelzet T, et al. Maternal complications induced by digoxin treatment of fetal tachycardia: A retrospective series of 18 cases. J Gynecol Obstet Hum Reprod 2018;47:35–38.
130. Yilmaz-Semerci S, Bornaun H, Kurnaz D, et al. Neonatal atrial flutter: Three cases and review of the literature. Turk J Pediatr 2018;60:306–309.
131. Cuneo BF, Zhao H, Strasburger JF, Ovadia M, Huhta JC, Wakai RT. Atrial and ventricular rate response and patterns of heart rate acceleration during maternal-fetal terbutaline treatment of fetal complete heart block. Am J Cardiol 2007; 100:661–665.
132. Robinson BV, Ettedgui JA, Sherman FS. Use of terbutaline in the treatment of complete heart block in the fetus. Cardiol Young 2001;11:683–686.
133. Murad SH, Tabsh KM, Conklin KA, et al. Verapamil: placental transfer and effects on maternal and fetal hemodynamics and atrioventricular conduction in the pregnant ewe. Anesthesiology 1985;62:49–53.
134. Cuneo BF, Ovadia M, Strasburger JF, et al. Prenatal diagnosis and in utero treatment of torsades de pointes associated with congenital long QT syndrome. Am J Cardiol 2003;91:1395–1398.
135. Al-Enazy S, Ali S, Albekairi N, El-Tawil M, Rytting E. Placental control of drug delivery. Adv Drug Deliv Rev 2017;116:63–72.
136. Mellander M, Gardiner H. Foetal therapy, what works? An overview. Cardiol Young 2014;24(Suppl 2):36–40.
137. Saksena, Camm AJ. Arrhythmias During Pregnancy. Electrophysiological Disorders of the Heart. Elsevier; 2012:1009–1025.
138. Roos Hesselink JW, Johnson MR. Care During Pregnancy. Pregnancy and Congenital Heart Disease. Springer; 2017:67–81.
139. Centers for Disease Control and Prevention. Medicine and pregnancy. Updated April 10, 2023, https://www.cdc.gov/pregnancy/meds/treatingfortwo/index.html.
140. U.S. Food and Drug Administration. Drug Safety and Availability. Updated April 28, 2023, https://www.fda.gov/drugs/drug-safety-and-availability.
141. U.S. Food and Drug Administration. Pregnancy. Updated April 11, 2022, https://www.fda.gov/consumers/womens-health-topics/pregnancy.
142. Walsh EP, Bar-Cohen Y, Batra AS, et al. Recommendations for advanced fellowship training in clinical pediatric and congenital electrophysiology: A report from the Training and Credentialing Committee of the Pediatric and Congenital Electrophysiology Society. Heart Rhythm 2013;10:775–781.
143. Elwyn G, Frosch D, Thomson R, et al. Shared decision making: a model for clinical practice. J Gen Intern Med 2012;27:1361–1367.
144. Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines on the Management of Adults With Congenital Heart Disease). Developed in Collaboration with the American Society of Echocardiography, Heart Rhythm Society, International Society for Adult Congenital Heart Disease, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol 2008;52:e143–e263.
145. Menard MK, Kilpatrick S, Saade G, et al. Levels of maternal care. Am J Obstet Gynecol 2015;212:259–271.
146. Dugas M, Shorten A, Dubé E, Wassef M, Bujold E, Chaillet N. Decision aid tools to support women's decision making in pregnancy and birth: a systematic review and meta-analysis. Soc Sci Med 2012;74:1968–1978.
147. Nieuwenhuijze MJ, Korstjens I, de Jonge A, de Vries R, Lagro-Janssen A. On speaking terms: a Delphi study on shared decision-making in maternity care. BMC Pregnancy Childbirth 2014;14:223.
148. Schilling RJ. Which patient should be referred to an electrophysiologist: Supraventricular tachycardia. Heart 2002;87:299–304.
149. Bai R, Napolitano C, Bloise R, Monteforte N, Priori SG. Yield of genetic screening in inherited cardiac channelopathies: how to prioritize access to genetic testing. Circ Arrhythm Electrophysiol 2009;2:6–15.
150. Hodes AR, Tichnell C, Te Riele AS, et al. Pregnancy course and outcomes in women with arrhythmogenic right ventricular cardiomyopathy. Heart 2016; 102:303–312.
151. Quarta G, Muir A, Pantazis A, et al. Familial evaluation in arrhythmogenic right ventricular cardiomyopathy: impact of genetics and revised task force criteria. Circulation 2011;123:2701–2709.
152. Gandjbakhch E, Varlet E, Duthoit G, et al. Pregnancy and newborn outcomes in arrhythmogenic right ventricular cardiomyopathy/dysplasia. Int J Cardiol 2018; 258:172–178.
153. Cuneo BF, Kaizer AM, Clur SA, et al. Mothers with long QT syndrome are at increased risk for fetal death: Findings from a multicenter international study. Am J Obstet Gynecol 2020;222:263.e261-263.e211.
154. Horigome H, Nagashima M, Sumitomo N, et al. Clinical characteristics and genetic background of congenital long-QT syndrome diagnosed in fetal, neonatal, and infantile life: a nationwide questionnaire survey in Japan. Circ Arrhythm Electrophysiol 2010;3:10–17.
155. Rosemond LR. Cardioversion during pregnancy. JAMA 1993;269:3167.
156. Cullhed I. Cardioversion during pregnancy. A case report. Acta Med Scand 1983;214:169–172.
157. Oktay C, Kesapli M, Altekin E. Wide-QRS complex tachycardia during pregnancy: treatment with cardioversion and review. Am J Emerg Med 2002; 20:492–493.
158. Wang YC, Chen CH, Su HY, Yu MH. The impact of maternal cardioversion on fetal haemodynamics. Eur J Obstet Gynecol Reprod Biol 2006;126:268–269.
159. Tromp CH, Nanne AC, Pernet PJ, Tukkie R, Bolte AC. Electrical cardioversion during pregnancy: safe or not? Neth Heart J 2011;19:134–136.
160. Pagan-Carlo LA, Spencer KT, Robertson CE, Dengler A, Birkett C, Kerber RE. Transthoracic defibrillation: importance of avoiding electrode placement directly on the female breast. J Am Coll Cardiol 1996;27:449–452.
161. Nanson J, Elcock D, Williams M, Deakin CD. Do physiological changes in pregnancy change defibrillation energy requirements? Br J Anaesth 2001; 87:237–239.
162. Ghosh N, Luk A, Derzko C, Dorian P, Chow CM. The acute treatment of maternal supraventricular tachycardias during pregnancy: a review of the literature. J Obstet Gynaecol Can 2011;33:17–23.
163. Damilakis J, Theocharopoulos N, Perisinakis K, et al. Conceptus radiation dose and risk from cardiac catheter ablation procedures. Circulation 2001; 104:893–897.
164. Szumowski L, Szufladowicz E, Orczykowski M, et al. Ablation of severe drug-resistant tachyarrhythmia during pregnancy. J Cardiovasc Electrophysiol 2010; 21:877–882.
165. Colletti PM, Lee KH, Elkayam U. Cardiovascular imaging of the pregnant patient. Am J Roentgenol 2013;200:515–521.
166. Sadek MM, Ramirez FD, Nery PB, et al. Completely nonfluoroscopic catheter ablation of left atrial arrhythmias and ventricular tachycardia. J Cardiovasc Electrophysiol 2019;30:78–88.
167. Field LM, Barton FL. The management of anaesthesia for caesarean section in a patient with paroxysmal ventricular tachycardia. Anaesthesia 1993; 48:593–595.
168. Singh V, Bhakta P, Hashmi J, Zaidi N. Cardioversion in late pregnancy: a case report. Acta Anaesthesiol Belg 2014;65:105–107.
169. Klepper I. Cardioversion in late pregnancy. The anaesthetic management of a case of Wolff-Parkinson-White syndrome. Anaesthesia 1981;36:611–616.
170. Kumakura M, Hara K, Sata T. Sevoflurane-associated torsade de pointes in a patient with congenital long QT syndrome genotype 2. J Clin Anesth 2016; 33:81–85.
171. Kim WH, Hur M, Park SK, et al. Comparison between general, spinal, epidural, and combined spinal-epidural anesthesia for cesarean delivery: a network meta-analysis. Int J Obstet Anesth 2019;37:5–15.
172. Delgado C, Ring L, Mushambi MC. General anaesthesia in obstetrics. BJA Educ 2020;20:201–207.
173. McLennan CE. Antecubital and femoral venous pressure in normal and toxemic pregnancy. Am J Obstet Gynecol 1943;45:568–591.
174. Ueland K, Novy MJ, Peterson EN, Metcalfe J. Maternal cardiovascular dynamics. IV. The influence of gestational age on the maternal cardiovascular response to posture and exercise. Am J Obstet Gynecol 1969;104:856–864.
175. Kundra P, Khanna S, Habeebullah S, Ravishankar M. Manual displacement of the uterus during Caesarean section. Anaesthesia 2007;62:460–465.
176. van Geijn HP, Copray FJ, Donkers DK, Bos MH. Diagnosis and management of intrapartum fetal distress. Eur J Obstet Gynecol Reprod Biol 1991; 42(suppl):S63–S72.
177. Drake E, Preston R, Douglas J. Brief review: anesthetic implications of long QT syndrome in pregnancy. Can J Anaesth 2007;54:561–572.
178. Fazio G, Vernuccio F, Grutta G, Re GL. Drugs to be avoided in patients with long QT syndrome: Focus on the anaesthesiological management. World J Cardiol 2013;5:87–93.
179. Easter SR, Rouse CE, Duarte V, et al. Planned vaginal delivery and cardiovascular morbidity in pregnant women with heart disease. Am J Obstet Gynecol 2020;222:77.e71-77.e11.
180. Hashimoto E, Kojima A, Kitagawa H, Matsuura H. Anesthetic management of a patient with type 1 long QT syndrome using combined epidural-spinal anes-

thesia for caesarean section: Perioperative approach based on ion channel function. J Cardiothorac Vasc Anesth 2020;34:465–469.
181. Loughnan PM. Digoxin excretion in human breast milk. J Pediatr 1978; 92:1019–1020.
182. McQuinn RL, Pisani A, Wafa S, et al. Flecainide excretion in human breast milk. Clin Pharmacol Ther 1990;48:262–267.
183. Strunge P, Frandsen J, Andreasen F. Amiodarone during pregnancy. Eur Heart J 1988;9:106–109.
184. Anderson P, Bondesson U, Mattiasson I, Johansson BW. Verapamil and norverapamil in plasma and breast milk during breast feeding. Eur J Clin Pharmacol 1987;31:625–627.
185. Okada M, Inoue H, Nakamura Y, Kishimoto M, Suzuki T. Excretion of diltiazem in human milk. N Engl J Med 1985;312:992–993.
186. Pittard WB 3rd, G H. Procainamide excretion in human milk. J Pediatr 1983; 102:631–633.
187. Kulas J, Lunell NO, Rosing U, Stéen B, Rane A. Atenolol and metoprolol. A comparison of their excretion into human breast milk. Acta Obstet Gynecol Scand Suppl 1984;118:65–69.
188. Taylor EA, Turner P. Anti-hypertensive therapy with propranolol during pregnancy and lactation. Postgrad Med J 1981;57:427–430.
189. O'Hare MF, Murnaghan GA, Russell CJ, Leahey WJ, Varma MP, McDevitt DG. Sotalol as a hypotensive agent in pregnancy. Br J Obstet Gynaecol 1980;87:814–820.
190. Eyal S, Kim JD, Anderson GD, et al. Atenolol pharmacokinetics and excretion in breast milk during the first 6 to 8 months postpartum. J Clin Pharmacol 2010; 50:1301–1309.
191. Khurana R, Bin Jardan YA, Wilkie J, Brocks DR. Breast milk concentrations of amiodarone, desethylamiodarone, and bisoprolol following short-term drug exposure: two case reports. J Clin Pharmacol 2014;54:828–831.
192. Ryu RJ, Eyal S, Easterling TR, et al. Pharmacokinetics of metoprolol during pregnancy and lactation. J Clin Pharmacol 2016;56:581–589.
193. Ruys TP, Roos-Hesselink JW, Pijuan-Domènech A, et al. Is a planned caesarean section in women with cardiac disease beneficial? Heart 2015; 101:530–536.
194. Tanaka H, Kamiya C, Katsuragi S, Tanaka K, Yoshimatsu J, Ikeda T. Effect of epidural anesthesia in labor; pregnancy with cardiovascular disease. Taiwan J Obstet Gynecol 2018;57:190–193.
195. Drugs and Lactation Database (LactMed). Amiodarone. National Institute of Child Health and Human Development; 2006, https://www.ncbi.nlm.nih.gov/books/NBK500560/. Accessed December 14, 2020.
196. Raviele A, Giada F, Bergfeldt L, et al. Management of patients with palpitations: a position paper from the European Heart Rhythm Association. Europace 2011; 13:920–934.
197. Walsh K, Hoffmayer K, Hamdan MH. Syncope: Diagnosis and management. Curr Probl Cardiol 2015;40:51–86.
198. Huang MH, Roeske WR, Hu H, Indik JH, Marcus FI. Postural position and neurocardiogenic syncope in late pregnancy. Am J Cardiol 2003;92:1252–1253.
199. Calkins H, Shyr Y, Frumin H, Schork A, Morady F. The value of the clinical history in the differentiation of syncope due to ventricular tachycardia, atrioventricular block, and neurocardiogenic syncope. Am J Med 1995;98:365–373.
200. Alboni P, Brignole M, Menozzi C, et al. Diagnostic value of history in patients with syncope with or without heart disease. J Am Coll Cardiol 2001; 37:1921–1928.
201. Sheldon R, Rose S, Connolly S, Ritchie D, Koshman ML, Frenneaux M. Diagnostic criteria for vasovagal syncope based on a quantitative history. Eur Heart J 2006;27:344–350.
202. van Dijk N, Boer KR, Colman N, et al. High diagnostic yield and accuracy of history, physical examination, and ECG in patients with transient loss of consciousness in FAST: the Fainting Assessment study. J Cardiovasc Electrophysiol 2008;19:48–55.
203. Chiu DT, Shapiro NI, Sun BC, Mottley JL, Grossman SA. Are echocardiography, telemetry, ambulatory electrocardiography monitoring, and cardiac enzymes in emergency department patients presenting with syncope useful tests? A preliminary investigation. J Emerg Med 2014;47:113–118.
204. Pérez-Rodon J, Martínez-Alday J, Barón-Esquivias G, et al. Prognostic value of the electrocardiogram in patients with syncope: Data from the Group For Syncope Study in the Emergency Room (GESINUR). Heart Rhythm 2014;11:2035–2044.
205. Grubb BP, Kosinski D, Samoil D, Pothoulakis A, Lorton M, Kip K. Postpartum syncope. Pacing Clin Electrophysiol 1995;18:1028–1031.
206. Kapoor WN. Evaluation and outcome of patients with syncope. Medicine (Baltimore) 1990;69:160–175.
207. Sarasin FP, Junod AF, Carballo D, Slama S, Unger PF, Louis-Simonet M. Role of echocardiography in the evaluation of syncope: a prospective study. Heart 2002;88:363–367.
208. Iglesias JF, Graf D, Forclaz A, Schlaepfer J, Fromer M, Pruvot E. Stepwise evaluation of unexplained syncope in a large ambulatory population. Pacing Clin Electrophysiol 2009;32(suppl 1):S202–S206.
209. Krahn AD, Klein GJ, Yee R, Skanes AC. Randomized assessment of syncope trial: conventional diagnostic testing versus a prolonged monitoring strategy. Circulation 2001;104:46–51.
210. Linzer M, Pritchett EL, Pontinen M, McCarthy E, Divine GW. Incremental diagnostic yield of loop electrocardiographic recorders in unexplained syncope. Am J Cardiol 1990;66:214–219.
211. Sivakumaran S, Krahn AD, Klein GJ, et al. A prospective randomized comparison of loop recorders versus Holter monitors in patients with syncope or presyncope. Am J Med 2003;115:1–5.
212. Sliwa K, Azibani F, Johnson MR, et al. Effectiveness of implanted cardiac rhythm recorders with electrocardiographic monitoring for detecting arrhythmias in pregnant women with symptomatic arrhythmia and/or structural heart disease: A randomized clinical trial. JAMA Cardiol 2020; 5:458–463.
213. Gibson PS, Powrie R, Peipert J. Prevalence of syncope and recurrent presyncope during pregnancy. Obstet Gynecol 2001;97:S41–S42.
214. Gonce-Mellgren A, Tamayo-Rojas O, Sanchez-Mart nez M, Salvia-Roiges D, Ramirez-Ruz J, Cararach-Ramoneda V. [Severe neonatal encephalopathy, secondary to a prolonged vasovagal episode in a woman 31 weeks pregnant]. Rev Neurol 2002;34:833–835.
215. Saqr L, Kumar MM. Neurocardiogenic syncope in the obstetric patient. Anaesthesia 2007;62:79–84.
216. Brent LR. The effect of embryonic and fetal exposure to x-ray, microwaves, and ultrasound: counseling the pregnant and nonpregnant patient about these risks. Semin Oncol 1989;16:347–368.
217. Twidale N, Tonkin AM. Clinical electrophysiology study in patients with syncope of undetermined etiology. Aust N Z J Med 1987;17:512–517.
218. Efstathopoulos EP, Katritsis DG, Kottou S, et al. Patient and staff radiation dosimetry during cardiac electrophysiology studies and catheter ablation procedures: A comprehensive analysis. Europace 2006;8:443–448.
219. Mendu ML, McAvay G, Lampert R, Stoehr J, Tinetti ME. Yield of diagnostic tests in evaluating syncopal episodes in older patients. Arch Intern Med 2009; 169:1299–1305.
220. Soteriades ES, Evans JC, Larson MG, et al. Incidence and prognosis of syncope. N Engl J Med 2002;347:878–885.
221. Bamber JH, Dresner M. Aortocaval compression in pregnancy: the effect of changing the degree and direction of lateral tilt on maternal cardiac output. Anesth Analg 2003;97:256–258. table of contents.
222. Humphries A, Mirjalili SA, Tarr GP, Thompson JMD, Stone P. Hemodynamic changes in women with symptoms of supine hypotensive syndrome. Acta Obstet Gynecol Scand 2020;99:631–636.
223. Anley C, Noakes T, Collins M, Schwellnus MP. A comparison of two treatment protocols in the management of exercise-associated postural hypotension: a randomised clinical trial. Br J Sports Med 2011;45:1113–1118.
224. McKenzie AG. Researches on supine hypotension in pregnancy. International Congress Series 2002;1242:597–601.
225. Lee MS, Chen W, Zhang Z, et al. Atrial fibrillation and atrial flutter in pregnant women-a population-based study. J Am Heart Assoc 2016;5:e003182.
226. Salam AM, Ertekin E, van Hagen IM, et al. Atrial fibrillation or flutter during pregnancy in patients with structural heart disease: Data from the ROPAC (Registry on Pregnancy and Cardiac Disease). JACC Clin Electrophysiol 2015; 1:284–292.
227. Chang SH, Kuo CF, Chou IJ, et al. Outcomes associated with paroxysmal supraventricular tachycardia during pregnancy. Circulation 2017;135:616–618.
228. Klein V, Repke JT. Supraventricular tachycardia in pregnancy: cardioversion with verapamil. Obstet Gynecol 1984;63:16S–18S.
229. Allen NM, Page RL. Procainamide administration during pregnancy. Clin Pharm 1993;12:58–60.
230. Robins K, Lyons G. Supraventricular tachycardia in pregnancy. Br J Anaesth 2004;92:140–143.
231. Waxman MB, Wald RW, Sharma AD, Huerta F, Cameron DA. Vagal techniques for termination of paroxysmal supraventricular tachycardia. Am J Cardiol 1980;46:655–664.
232. Jaeggi E, Fouron JC, Drblik SP. Fetal atrial flutter: diagnosis, clinical features, treatment, and outcome. J Pediatr 1998;132:335–339.
233. Tavsanoglu S, Ozenel E. Ice-water washcloth rather than facial immersion (diving reflex) for supraventricular tachycardia in adults. Am J Cardiol 1985; 56:1003.
234. Yaksh A, van der Does LJ, Lanters EA, de Groot NM. Pharmacological therapy of tachyarrhythmias during pregnancy. Arrhythm Electrophysiol Rev 2016; 5:41–44.

235. Widerhorn J, Widerhorn AL, Rahimtoola SH, Elkayam U. WPW syndrome during pregnancy: increased incidence of supraventricular arrhythmias. Am Heart J 1992;123:796–798.
236. Gleicher N, Meller J, Sandler RZ, Sullum S. Wolff-Parkinson-White syndrome in pregnancy. Obstet Gynecol 1981;58:748–752.
237. Wang NC, Shen C, McLaughlin TJ, et al. Maternal focal atrial tachycardia during pregnancy: A systematic review. J Cardiovasc Electrophysiol 2020; 31:2982–2997.
238. Libardoni M, Piovan D, Busato E, Padrini R. Transfer of propafenone and 5-OH-propafenone to foetal plasma and maternal milk. Br J Clin Pharmacol 1991; 32:527–528.
239. Murphy JJ, Hutchon DJ. Incessant atrial tachycardia accelerated by pregnancy. Br Heart J 1992;68:342.
240. Schroeder JS, Harrison DC. Repeated cardioversion during pregnancy: Treatment of refractory paroxysmal atrial tachycardia during 3 successive pregnancies. Am J Cardiol 1971;27:445–446.
241. Hubbard WN, Jenkins BA, Ward DE. Persistent atrial tachycardia in pregnancy. Br Med J (Clin Res Ed) 1983;287:327.
242. Echt DS, Liebson PR, Mitchell LB, et al. Mortality and morbidity in patients receiving encainide, flecainide, or placebo. N Engl J Med 1991; 324:781–788.
243. Driver K, Chisholm CA, Darby AE, Malhotra R, Dimarco JP, Ferguson JD. Catheter ablation of arrhythmia during pregnancy. J Cardiovasc Electrophysiol 2015;26:698–702.
244. Chen G, Sun G, Xu R, et al. Zero-fluoroscopy catheter ablation of severe drug-resistant arrhythmia guided by Ensite NavX system during pregnancy: Two case reports and literature review. Medicine (Baltimore) 2016;95:e4487.
245. Sanchez Diaz CJ, Gonzalez Carmona VM, Ruesga Zamora E, Monteverde Grether CA. [Electric cardioversion in the emergency service: Experience in 1000 cases]. Arch Inst Cardiol Mex 1987;57:387–394.
246. Byerly WG, Hartmann A, Foster DE, Tannenbaum AK. Verapamil in the treatment of maternal paroxysmal supraventricular tachycardia. Ann Emerg Med 1991;20:552–554.
247. Xu Z, Fan J, Luo X, et al. Anticoagulation regimens during pregnancy in patients with mechanical heart valves: A systematic review and meta-analysis. Can J Cardiol 2016;32:1248.e1241–1248.e1249.
248. Kockova R, Kocka V, Kiernan T, Fahy GJ. Ibutilide-induced cardioversion of atrial fibrillation during pregnancy. J Cardiovasc Electrophysiol 2007; 18:545–547.
249. Lewis G, Currie P. Atrial fibrillation during pregnancy: cardioversion with flecainide. Br J Hosp Med (Lond) 2015;76:720–721.
250. Wichman K, Ryden G, Karlberg BE. A placebo controlled trial of metoprolol in the treatment of hypertension in pregnancy. Scand J Clin Lab Invest Suppl 1984; 169:90–95.
251. Frohn-Mulder IM, Stewart PA, Witsenburg M, Den Hollander NS, Wladimiroff JW, Hess J. The efficacy of flecainide versus digoxin in the management of fetal supraventricular tachycardia. Prenat Diagn 1995; 15:1297–1302.
252. Ebenroth ES, Cordes TM, Darragh RK. Second-line treatment of fetal supraventricular tachycardia using flecainide acetate. Pediatr Cardiol 2001;22:483–487.
253. Davis RL, Eastman D, McPhillips H, et al. Risks of congenital malformations and perinatal events among infants exposed to calcium channel and beta-blockers during pregnancy. Pharmacoepidemiol Drug Saf 2011;20:138–145.
254. Shah A, Moon-Grady A, Bhogal N, et al. Effectiveness of sotalol as first-line therapy for fetal supraventricular tachyarrhythmias. Am J Cardiol 2012; 109:1614–1618.
255. Meidahl Petersen K, Jimenez-Solem E, Andersen JT, et al. Beta-blocker treatment during pregnancy and adverse pregnancy outcomes: a nationwide population-based cohort study. BMJ Open 2012;2.
256. Oudijk MA, Michon MM, Kleinman CS, et al. Sotalol in the treatment of fetal dysrhythmias. Circulation 2000;101:2721–2726.
257. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: The Euro Heart Survey on Atrial Fibrillation. Chest 2010;137:263–272.
258. Heit JA, Kobbervig CE, James AH, et al. Trends in the incidence of venous thromboembolism during pregnancy or postpartum: a 30-year population-based study. Ann Intern Med 2005;143:697–706.
259. Alboni P, Botto GL, Baldi N, et al. Outpatient treatment of recent-onset atrial fibrillation with the "pill-in-the-pocket" approach. N Engl J Med 2004; 351:2384–2391.
260. De Rita F, Barozzi L, Franchi G, Faggian G, Mazzucco A, Luciani GB. Rescue extracorporeal life support for acute verapamil and propranolol toxicity in a neonate. Artif Organs 2011;35:416–420.
261. Smith G, Clark JM. Elimination of fluoroscopy use in a pediatric electrophysiology laboratory utilizing three-dimensional mapping. Pacing Clin Electrophysiol 2007;30:510–518.
262. Bigelow AM, Smith G, Clark JM. Catheter ablation without fluoroscopy: Current techniques and future direction. J Atr Fibrillation 2014;6:1066.
263. Kottkamp H, Hugl B, Krauss B, et al. Electromagnetic versus fluoroscopic mapping of the inferior isthmus for ablation of typical atrial flutter: A prospective randomized study. Circulation 2000;102:2082–2086.
264. Spector P, Reynolds MR, Calkins H, et al. Meta-analysis of ablation of atrial flutter and supraventricular tachycardia. Am J Cardiol 2009;104:671–677.
265. Sommer P, Bertagnolli L, Kircher S, et al. Safety profile of near-zero fluoroscopy atrial fibrillation ablation with non-fluoroscopic catheter visualization: experience from 1000 consecutive procedures. Europace 2018; 20:1952–1958.
266. Widerhorn J, Bhandari AK, Bughi S, Rahimtoola SH, Elkayam U. Fetal and neonatal adverse effects profile of amiodarone treatment during pregnancy. Am Heart J 1991;122:1162–1166.
267. Lameijer H, Aalberts JJJ, van Veldhuisen DJ, Meijer K, Pieper PG. Efficacy and safety of direct oral anticoagulants during pregnancy; a systematic literature review. Thromb Res 2018;169:123–127.
268. Beyer-Westendorf J, Tittl L, Bistervels I, et al. Safety of direct oral anticoagulant exposure during pregnancy: a retrospective cohort study. Lancet Haematol 2020;7:e884–e891.
269. Natale A, Davidson T, Geiger MJ, Newby K. Implantable cardioverter-defibrillators and pregnancy: a safe combination? Circulation 1997; 96:2808–2812.
270. Puri A, Sethi R, Singh B, et al. Peripartum cardiomyopathy presenting with ventricular tachycardia: a rare presentation. Indian Pacing Electrophysiol J 2009; 9:186–189.
271. Wilber DJ, Baerman J, Olshansky B, Kall J, Kopp D. Adenosine-sensitive ventricular tachycardia. Clinical characteristics and response to catheter ablation. Circulation 1993;87:126–134.
272. Cleary-Goldman J, Salva CR, Infeld JI, Robinson JN. Verapamil-sensitive idiopathic left ventricular tachycardia in pregnancy. J Matern Fetal Neonatal Med 2003;14:132–135.
273. Nakagawa M, Katou S, Ichinose M, et al. Characteristics of new-onset ventricular arrhythmias in pregnancy. J Electrocardiol 2004;37:47–53.
274. Makhija A, Sharada K, Hygriv Rao B, Thachil A, Narsimhan C. Hormone sensitive idiopathic ventricular tachycardia associated with pregnancy: successful induction with progesterone and radiofrequency ablation. J Cardiovasc Electrophysiol 2011;22:95–98.
275. Kotchetkov R, Patel A, Salehian O. Ventricular tachycardia in pregnant patients. Clin Med Insights Cardiol 2010;4:39–44.
276. Gorgels AP, van den Dool A, Hofs A, et al. Comparison of procainamide and lidocaine in terminating sustained monomorphic ventricular tachycardia. Am J Cardiol 1996;78:43–46.
277. Komura S, Chinushi M, Furushima H, et al. Efficacy of procainamide and lidocaine in terminating sustained monomorphic ventricular tachycardia. Circ J 2010;74:864–869.
278. Ortiz M, Martin A, Arribas F, et al. Randomized comparison of intravenous procainamide vs. intravenous amiodarone for the acute treatment of tolerated wide QRS tachycardia: the PROCAMIO study. Eur Heart J 2017; 38:1329–1335.
279. Boule S, Ovart L, Marquie C, et al. Pregnancy in women with an implantable cardioverter-defibrillator: is it safe? Europace 2014;16:1587–1594.
280. Tuzcu V, Gul EE, Erdem A, et al. Cardiac interventions in pregnant patients without fluoroscopy. Pediatr Cardiol 2015;36:1304–1307.
281. Payne J, Lo M, Paydak H, Maskoun W. Near-zero fluoroscopy implantation of dual-chamber pacemaker in pregnancy using electroanatomic mapping. HeartRhythm Case Rep 2017;3:205–209.
282. Chua KCM, Lim ETS, Chong DTT, Tan BY, Ho KL, Ching CK. Implantation of a dual-chamber permanent pacemaker in a pregnant patient guided by intracardiac echocardiography and electroanatomic mapping. HeartRhythm Case Rep 2017;3:542–545.
283. Schuler PK, Herrey A, Wade A, et al. Pregnancy outcome and management of women with an implantable cardioverter defibrillator: a single centre experience. Europace 2012;14:1740–1745.
284. Miyoshi T, Kamiya CA, Katsuragi S, et al. Safety and efficacy of implantable cardioverter-defibrillator during pregnancy and after delivery. Circ J 2013; 77:1166–1170.
285. Ertekin E, van Hagen IM, Salam AM, et al. Ventricular tachyarrhythmia during pregnancy in women with heart disease: Data from the ROPAC, a registry from the European Society of Cardiology. Int J Cardiol 2016; 220:131–136.

286. Gregg AR, Tomich PG. Mexilitene use in pregnancy. J Perinatol 1988;8:33–35.
287. Kambiré Y, Konaté L, Millogo GR, et al. Right ventricular outflow tract tachycardia worsened during pregnancy. Pan Afr Med J 2015;20:60.
288. Lahiri A, Srinath SC, Roshan J. Radiofrequency ablation of recurrent, drug refractory, left posterior fascicular ventricular tachycardia in a pregnant lady without the use of fluoroscopy. Indian Pacing Electrophysiol J 2019; 19:119–124.
289. Saltzberg MT, Szymkiewicz S, Bianco NR. Characteristics and outcomes of peripartum versus nonperipartum cardiomyopathy in women using a wearable cardiac defibrillator. J Card Fail 2012;18:21–27.
290. Duncker D, Haghikia A, Konig T, et al. Risk for ventricular fibrillation in peripartum cardiomyopathy with severely reduced left ventricular function-value of the wearable cardioverter/defibrillator. Eur J Heart Fail 2014;16:1331–1336.
291. Hankins GD, Wendel GD Jr, Leveno KJ, Stoneham J. Myocardial infarction during pregnancy: a review. Obstet Gynecol 1985;65:139–146.
292. Elkayam U, Goodwin TM. Adenosine therapy for supraventricular tachycardia during pregnancy. Am J Cardiol 1995;75:521–523.
293. Kochhar PK, Ghosh P. Ventricular tachycardia in a primigravida with hyperemesis gravidarum. J Obstet Gynaecol Res 2018;44:1308–1312.
294. Strewe C, Fichtner S. [Completely subcutaneous implantable cardioverter defibrillator: Care of S-ICD wearers during childbirth]. Anaesthesist 2015; 64:843–845.
295. Magee LA, Nulman I, Rovet JF, Koren G. Neurodevelopment after in utero amiodarone exposure. Neurotoxicol Teratol 1999;21:261–265.
296. McNamara DM, Elkayam U, Alharethi R, et al. Clinical outcomes for peripartum cardiomyopathy in North America: results of the IPAC study (investigations of pregnancy-associated cardiomyopathy). J Am Coll Cardiol 2015; 66:905–914.
297. Keepanasseril A, Maurya DK, Suriya Y, Selvaraj R. Complete atrioventricular block in pregnancy: report of seven pregnancies in a patient without pacemaker. BMJ Case Rep 2015;2015:bcr2014208618.
298. Mangrum JM, DiMarco JP. The evaluation and management of bradycardia. N Engl J Med 2000;342:703–709.
299. Hartz J, Clark BC, Ito S, Sherwin ED, Berul CI. Transvenous nonfluoroscopic pacemaker implantation during pregnancy guided by 3-dimensional electroanatomic mapping. HeartRhythm Case Rep 2017;3:490–492.
300. Kandolin R, Lehtonen J, Kupari M. Cardiac sarcoidosis and giant cell myocarditis as causes of atrioventricular block in young and middle-aged adults. Circ Arrhythm Electrophysiol 2011;4:303–309.
301. Nery PB, Beanlands RS, Nair GM, et al. Atrioventricular block as the initial manifestation of cardiac sarcoidosis in middle-aged adults. J Cardiovasc Electrophysiol 2014;25:875–881.
302. Dalvi BV, Chaudhuri A, Kulkarni HL, Kale PA. Therapeutic guidelines for congenital complete heart-block presenting in pregnancy. Obstet Gynecol 1992;79:802–804.
303. Thaman R, Curtis S, Faganello G, et al. Cardiac outcome of pregnancy in women with a pacemaker and women with untreated atrioventricular conduction block. Europace 2011;13:859–863.
304. Sundararaman L, Hochman Cohn J, Ranasinghe JS. Complete heart block in pregnancy: case report, analysis, and review of anesthetic management. J Clin Anesth 2016;33:58–61.
305. Strasberg B, Amat YLF, Dhingra RC, et al. Natural history of chronic second-degree atrioventricular nodal block. Circulation 1981;63:1043–1049.
306. Hidaka N, Chiba Y, Fukushima K, Wake N. Pregnant women with complete atrioventricular block: Perinatal risks and review of management. Pacing Clin Electrophysiol 2011;34:1161–1176.
307. Hidaka N, Chiba Y, Kurita T, Satoh S, Nakano H. Is intrapartum temporary pacing required for women with complete atrioventricular block? An analysis of seven cases. BJOG 2006;113:605–607.
308. Bluemke DA, Achenbach S, Budoff M, et al. Noninvasive coronary artery imaging: magnetic resonance angiography and multidetector computed tomography angiography: a scientific statement from the American Heart Association committee on cardiovascular imaging and intervention of the council on cardiovascular radiology and intervention, and the councils on clinical cardiology and cardiovascular disease in the young. Circulation 2008;118:586–606.
309. ACOG committee opinion no. 723: Guidelines for diagnostic imaging during pregnancy and lactation. Obstet Gynecol 2017;130:e210–e216.
310. Raikhelkar J, Schumann R. Temporary pacemaker and spinal anesthesia for cesarean section in a patient with spontaneous complete heart block during pregnancy. Anesthesiology 2004;100:B66-B66.
311. Mendelson LC. Disorders of the heartbeat during pregnancy. Am J Obstet Gynecol 1956;72:1268–1301.
312. Panchal AR, Bartos JA, Cabañas JG, et al. Part 3: Adult basic and advanced life support: 2020 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2020; 142:S366–s468.
313. Shields LE, Wiesner S, Klein C, Pelletreau B, Hedriana HL. Use of Maternal Early Warning Trigger tool reduces maternal morbidity. Am J Obstet Gynecol 2016;214:527.e521–527.e526.
314. Lipman SS, Daniels KI, Carvalho B, et al. Deficits in the provision of cardiopulmonary resuscitation during simulated obstetric crises. Am J Obstet Gynecol 2010;203:179.e171–179.e175.
315. Fisher N, Eisen LA, Bayya JV, et al. Improved performance of maternal-fetal medicine staff after maternal cardiac arrest simulation-based training. Am J Obstet Gynecol 2011;205:239.e231–239.e235.
316. Fransen AF, van de Ven J, Merien AE, et al. Effect of obstetric team training on team performance and medical technical skills: a randomised controlled trial. BJOG 2012;119:1387–1393.
317. Beckett VA, Knight M, Sharpe P. The CAPS Study: incidence, management and outcomes of cardiac arrest in pregnancy in the UK: a prospective, descriptive study. BJOG 2017;124:1374–1381.
318. Butcher M, Ip J, Bushby D, Yentis SM. Efficacy of cardiopulmonary resuscitation in the supine position with manual displacement of the uterus vs lateral tilt using a firm wedge: a manikin study. Anaesthesia 2014;69:868–871.
319. Holmes S, Kirkpatrick ID, Zelop CM, Jassal DS. MRI evaluation of maternal cardiac displacement in pregnancy: implications for cardiopulmonary resuscitation. Am J Obstet Gynecol 2015;213:401.e401-405.
320. Lipman S, Daniels K, Cohen SE, Carvalho B. Labor room setting compared with the operating room for simulated perimortem cesarean delivery: a randomized controlled trial. Obstet Gynecol 2011;118:1090–1094.
321. Lipman SS, Wong JY, Arafeh J, Cohen SE, Carvalho B. Transport decreases the quality of cardiopulmonary resuscitation during simulated maternal cardiac arrest. Anesth Analg 2013;116:162–167.
322. Katz VL, Dotters DJ, Droegemueller W. Perimortem cesarean delivery. Obstet Gynecol 1986;68:571–576.
323. Einav S, Kaufman N, Sela HY. Maternal cardiac arrest and perimortem caesarean delivery: evidence or expert-based? Resuscitation 2012; 83:1191–1200.
324. Baghirzada L, Balki M. Maternal cardiac arrest in a tertiary care centre during 1989-2011: a case series. Can J Anaesth 2013;60:1077–1084.
325. Rees GA, Willis BA. Resuscitation in late pregnancy. Anaesthesia 1988; 43:347–349.
326. Tracy TS, Venkataramanan R, Glover DD, Caritis SN. Temporal changes in drug metabolism (CYP1A2, CYP2D6 and CYP3A Activity) during pregnancy. Am J Obstet Gynecol 2005;192:633–639.
327. Feghali M, Venkataramanan R, Caritis S. Pharmacokinetics of drugs in pregnancy. Semin Perinatol 2015;39:512–519.
328. Katz V, Balderston K, DeFreest M. Perimortem cesarean delivery: were our assumptions correct? Am J Obstet Gynecol 2005;192:1916–1920; discussion 1920-1911.
329. Parker J, Balis N, Chester S, Adey D. Cardiopulmonary arrest in pregnancy: successful resuscitation of mother and infant following immediate caesarean section in labour ward. Aust N Z J Obstet Gynaecol 1996;36:207–210.
330. Siu SC, Sermer M, Colman JM, et al. Prospective multicenter study of pregnancy outcomes in women with heart disease. Circulation 2001; 104:515–521.
331. Drenthen W, Boersma E, Balci A, et al. Predictors of pregnancy complications in women with congenital heart disease. Eur Heart J 2010;31:2124–2132.
332. Roos-Hesselink JW, Ruys TP, Stein JI, et al. Outcome of pregnancy in patients with structural or ischaemic heart disease: results of a registry of the European Society of Cardiology. Eur Heart J 2013;34:657–665.
333. Tateno S, Niwa K, Nakazawa M, et al. Arrhythmia and conduction disturbances in patients with congenital heart disease during pregnancy: multicenter study. Circ J 2003;67:992–997.
334. Drenthen W, Pieper PG, Roos-Hesselink JW, et al. Outcome of pregnancy in women with congenital heart disease: A literature review. J Am Coll Cardiol 2007;49:2303–2311.
335. Wu MH, Lu CW, Chen HC, Kao FY, Huang SK. Adult congenital heart disease in a nationwide population 2000-2014: Epidemiological trends, arrhythmia, and standardized mortality ratio. J Am Heart Assoc 2018;7:e007907.
336. Kaemmerer H, Fratz S, Bauer U, et al. Emergency hospital admissions and three-year survival of adults with and without cardiovascular surgery for congenital cardiac disease. J Thorac Cardiovasc Surg 2003; 126:1048–1052.
337. Kaemmerer H, Bauer U, Pensl U, et al. Management of emergencies in adults with congenital cardiac disease. Am J Cardiol 2008;101:521–525.
338. Bouchardy J, Therrien J, Pilote L, et al. Atrial arrhythmias in adults with congenital heart disease. Circulation 2009;120:1679–1686.

339. Silka MJ, Hardy BG, Menashe VD, Morris CD. A population-based prospective evaluation of risk of sudden cardiac death after operation for common congenital heart defects. J Am Coll Cardiol 1998;32:245–251.
340. Gouton M, Nizard J, Patel M, et al. Maternal and fetal outcomes of pregnancy with Fontan circulation: A multicentric observational study. Int J Cardiol 2015;187:84–89.
341. Pundi KN, Pundi K, Johnson JN, et al. Contraception practices and pregnancy outcome in patients after Fontan operation. Congenit Heart Dis 2016;11:63–70.
342. Cauldwell M, Steer PJ, Bonner S, et al. Retrospective UK multicentre study of the pregnancy outcomes of women with a Fontan repair. Heart 2018; 104:401–406.
343. Garcia Ropero A, Baskar S, Roos Hesselink JW, et al. Pregnancy in women with a Fontan circulation: A systematic review of the literature. Circ Cardiovasc Qual Outcomes 2018;11:e004575.
344. Feltes TF, Friedman RA. Transesophageal echocardiographic detection of atrial thrombi in patients with nonfibrillation atrial tachyarrhythmias and congenital heart disease. J Am Coll Cardiol 1994;24:1365–1370.
345. Khairy P, Fernandes SM, Mayer JE, et al. Long-term survival, modes of death, and predictors of mortality in patients with Fontan surgery. Circulation 2008; 117:85–92.
346. Ammash NM, Phillips SD, Hodge DO, et al. Outcome of direct current cardioversion for atrial arrhythmias in adults with congenital heart disease. Int J Cardiol 2012;154:270–274.
347. Garson A Jr, Bink-Boelkens M, et al. Atrial flutter in the young: a collaborative study of 380 cases. J Am Coll Cardiol 1985;6:871–878.
348. Rhodes LA, Walsh EP, Gamble WJ, Triedman JK, Saul JP. Benefits and potential risks of atrial antitachycardia pacing after repair of congenital heart disease. Pacing Clin Electrophysiol 1995;18:1005–1016.
349. Zielonka B, Kim YY, Supple GE, et al. Improvement in ventricular function with rhythm control of atrial arrhythmias may delay the need for atrioventricular valve surgery in adults with congenital heart disease. Congenit Heart Dis 2019; 14:931–938.
350. Kozluk E, Piatkowska A, Kiliszek M, et al. Catheter ablation of cardiac arrhythmias in pregnancy without fluoroscopy: A case control retrospective study. Adv Clin Exp Med 2017;26:129–134.
351. Foster CJ, Love HG. Amiodarone in pregnancy. Case report and review of the literature. Int J Cardiol 1988;20:307–316.
352. Triedman JK, DeLucca JM, Alexander ME, Berul CI, Cecchin F, Walsh EP. Prospective trial of electroanatomically guided, irrigated catheter ablation of atrial tachycardia in patients with congenital heart disease. Heart Rhythm 2005; 2:700–705.
353. Labombarda F, Hamilton R, Shohoudi A, et al. Increasing prevalence of atrial fibrillation and permanent atrial arrhythmias in congenital heart disease. J Am Coll Cardiol 2017;70:857–865.
354. Silversides CK, Colman JM, Sermer M, Siu SC. Cardiac risk in pregnant women with rheumatic mitral stenosis. Am J Cardiol 2003;91:1382–1385.
355. Ducas RA, Javier DA, D'Souza R, Silversides CK, Tsang W. Pregnancy outcomes in women with significant valve disease: a systematic review and meta-analysis. Heart 2020;106:512–519.
356. van Hagen IM, Thorne SA, Taha N, et al. Pregnancy Outcomes in Women With Rheumatic Mitral Valve Disease: Results From the Registry of Pregnancy and Cardiac Disease. Circulation 2018;137:806–816.
357. Diao M, Kane A, Ndiaye MB, et al. Pregnancy in women with heart disease in sub-Saharan Africa. Arch Cardiovasc Dis 2011;104:370–374.
358. D'Souza R, Silversides CK, McLintock C. Optimal anticoagulation for pregnant women with mechanical heart valves. Semin Thromb Hemost 2016;42:798–804.
359. Manning WJ, Silverman DI, Keighley CS, Oettgen P, Douglas PS. Transesophageal echocardiographically facilitated early cardioversion from atrial fibrillation using short-term anticoagulation: final results of a prospective 4.5-year study. J Am Coll Cardiol 1995;25:1354–1361.
360. Rowe JC, Bland EF, Sprague HB, White PD. The course of mitral stenosis without surgery: ten- and twenty-year perspectives. Ann Intern Med 1960; 52:741–749.
361. Albers GW, Dalen JE, Laupacis A, Manning WJ, Petersen P, Singer DE. Antithrombotic therapy in atrial fibrillation. Chest 2001;119:194S–206S.
362. Perez-Gomez F, Salvador A, Zumalde J, et al. Effect of antithrombotic therapy in patients with mitral stenosis and atrial fibrillation: a sub-analysis of NASPEAF randomized trial. Eur Heart J 2006;27:960–967.
363. Murray B. Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C): a review of molecular and clinical literature. J Genet Couns 2012; 21:494–504.
364. Bauce B, Daliento L, Frigo G, Russo G, Nava A. Pregnancy in women with arrhythmogenic right ventricular cardiomyopathy/dysplasia. Eur J Obstet Gynecol Reprod Biol 2006;127:186–189.
365. Castrini AI, Lie OH, Leren IS, et al. Number of pregnancies and subsequent phenotype in a cross-sectional cohort of women with arrhythmogenic cardiomyopathy. Eur Heart J Cardiovasc Imaging 2019;20:192–198.
366. Marcus FI, Edson S, Towbin JA. Genetics of arrhythmogenic right ventricular cardiomyopathy: a practical guide for physicians. J Am Coll Cardiol 2013; 61:1945–1948.
367. Ermakov S, Scheinman M. Arrhythmogenic right ventricular cardiomyopathy—antiarrhythmic therapy. Arrhythm Electrophysiol Rev 2015;4:86–89.
368. Ermakov S, Gerstenfeld EP, Svetlichnaya Y, Scheinman MM. Use of flecainide in combination antiarrhythmic therapy in patients with arrhythmogenic right ventricular cardiomyopathy. Heart Rhythm 2017;14:564–569.
369. Marcus GM, Glidden DV, Polonsky B, et al. Efficacy of antiarrhythmic drugs in arrhythmogenic right ventricular cardiomyopathy: A report from the North American ARVC Registry. J Am Coll Cardiol 2009;54:609–615.
370. Jensen MK, Havndrup O, Christiansen M, et al. Penetrance of hypertrophic cardiomyopathy in children and adolescents: a 12-year follow-up study of clinical screening and predictive genetic testing. Circulation 2013;127:48–54.
371. Ho CY, Day SM, Ashley EA, et al. Genotype and lifetime burden of disease in hypertrophic cardiomyopathy: Insights from the Sarcomeric Human Cardiomyopathy Registry (SHaRe). Circulation 2018;138:1387–1398.
372. Autore C, Conte MR, Piccininno M, et al. Risk associated with pregnancy in hypertrophic cardiomyopathy. J Am Coll Cardiol 2002;40:1864–1869.
373. Thaman R, Varnava A, Hamid MS, et al. Pregnancy related complications in women with hypertrophic cardiomyopathy. Heart 2003;89:752–756.
374. Avila WS, Amaral FM, Ramires JA, et al. Influence of pregnancy on clinical course and fetal outcome of women with hypertrophic cardiomyopathy. Arq Bras Cardiol 2007;88:480–485.
375. Schinkel AF. Pregnancy in women with hypertrophic cardiomyopathy. Cardiol Rev 2014;22:217–222.
376. Goland S, van Hagen IM, Elbaz-Greener G, et al. Pregnancy in women with hypertrophic cardiomyopathy: data from the European Society of Cardiology initiated Registry of Pregnancy and Cardiac disease (ROPAC). Eur Heart J 2017; 38:2683–2690.
377. Maron BJ, Maron MS, Semsarian C. Genetics of hypertrophic cardiomyopathy after 20 years: clinical perspectives. J Am Coll Cardiol 2012;60:705–715.
378. Marian AJ, Braunwald E. Hypertrophic cardiomyopathy: Genetics, pathogenesis, clinical manifestations, diagnosis, and therapy. Circ Res 2017; 121:749–770.
379. Deal B, Wolff G, Gelband H. Fetal arrhythmias. Current Concepts in Diagnosis and Management of Arrhythmias in Infants and Children: Futura Publishing Company, Inc; 1998.
380. Naheed ZJ, Strasburger JF, Deal BJ, Benson DW Jr, Gidding SS. Fetal tachycardia: mechanisms and predictors of hydrops fetalis. J Am Coll Cardiol 1996;27:1736–1740.
381. Lisowski LA, Verheijen PM, Benatar AA, et al. Atrial flutter in the perinatal age group: diagnosis, management and outcome. J Am Coll Cardiol 2000; 35:771–777.
382. Krapp M, Kohl T, Simpson JM, Sharland GK, Katalinic A, Gembruch U. Review of diagnosis, treatment, and outcome of fetal atrial flutter compared with supraventricular tachycardia. Heart 2003;89:913–917.
383. Ekman-Joelsson BM, Mellander M, Lagnefeldt L, Sonesson SE. Foetal tachyarrhythmia treatment remains challenging even if the vast majority of cases have a favourable outcome. Acta Paediatr 2015;104:1090–1097.
384. Sridharan S, Sullivan I, Tomek V, et al. Flecainide versus digoxin for fetal supraventricular tachycardia: Comparison of two drug treatment protocols. Heart Rhythm 2016;13:1913–1919.
385. Texter KM, Kertesz NJ, Friedman RA, Fenrich AL Jr. Atrial flutter in infants. J Am Coll Cardiol 2006;48:1040–1046.
386. Hinkle KA, Peyvandi S, Stiver C, et al. Postnatal outcomes of fetal supraventricular tachycardia: A multicenter study. Pediatr Cardiol 2017;38:1317–1323.
387. Kleinman CS, Hobbins JC, Jaffe CC, Lynch DC, Talner NS. Echocardiographic studies of the human fetus: prenatal diagnosis of congenital heart disease and cardiac dysrhythmias. Pediatrics 1980;65:1059–1067.
388. Copel JA, Liang RI, Demasio K, Ozeren S, Kleinman CS. The clinical significance of the irregular fetal heart rhythm. Am J Obstet Gynecol 2000; 182:813–819.
389. Hansmann M, Gembruch U, Bald R, Manz M, Redel DA. Fetal tachyarrhythmias: transplacental and direct treatment of the fetus-a report of 60 cases. Ultrasound Obstet Gynecol 1991;1:162–168.
390. Kang SL, Howe D, Coleman M, Roman K, Gnanapragasam J. Foetal supraventricular tachycardia with hydrops fetalis: a role for direct intraperitoneal amiodarone. Cardiol Young 2015;25:447–453.
391. Capone CA, Gebb J, Dar P, Shenoy RU. Favorable neurodevelopmental outcome in a hypothyroid neonate following intracordal amiodarone for cardio-

version of refractory supraventricular tachycardia in a fetus. J Neonatal Perinatal Med 2014;7:305–309.
392. Lin PH, Wu HH, Tsai HD, Hsieh CT. Successful treatment of atrial flutter by repeated intraperitoneal and intra-amniotic injections of amiodarone in a fetus with hydrops. Taiwan J Obstet Gynecol 2016;55:434–436.
393. Owen J, Colvin EV, Davis RO. Fetal death after successful conversion of fetal supraventricular tachycardia with digoxin and verapamil. Am J Obstet Gynecol 1988;158:1169–1170.
394. Schiff S, Sacchetti A, Santiago J, Beatty L. Lack of fetal effect from adenosine administration in a pregnant patient. Am J Emerg Med 2019; 37:1604.e1601–1604.e1602.
395. Zhao H, Cuneo BF, Strasburger JF, Huhta JC, Gotteiner NL, Wakai RT. Electrophysiological characteristics of fetal atrioventricular block. J Am Coll Cardiol 2008;51:77–84.
396. Miyake CY, Del Nido PJ, Alexander ME, et al. Cardiac tumors and associated arrhythmias in pediatric patients, with observations on surgical therapy for ventricular tachycardia. J Am Coll Cardiol 2011;58:1903–1909.
397. Peters C, Wacker-Gussmann A, Strasburger JF, et al. Electrophysiologic features of fetal ventricular aneurysms and diverticula. Prenat Diagn 2015; 35:129–136.
398. Simpson JM, Maxwell D, Rosenthal E, Gill H. Fetal ventricular tachycardia secondary to long QT syndrome treated with maternal intravenous magnesium: case report and review of the literature. Ultrasound Obstet Gynecol 2009;34:475–480.
399. Cuneo BF, Strasburger JF, Niksch A, Ovadia M, Wakai RT. An expanded phenotype of maternal SSA/SSB antibody-associated fetal cardiac disease. J Matern Fetal Neonatal Med 2009;22:233–238.
400. Bonnin A, Tassin M, Vauloup-Fellous C, et al. Case of a healthy infant born following antenatal enterovirus myocarditis and hydrops. J Clin Virol 2014; 61:459–462.
401. Chinushi M, Sugiura H, Komura S, et al. Effects of intravenous magnesium in a prolonged QT interval model of polymorphic ventricular tachycardia focus on transmural ventricular repolarization. Pacing Clin Electrophysiol 2005; 28:844–850.
402. Friedman DM, Kim MY, Copel JA, Llanos C, Davis C, Buyon JP. Prospective evaluation of fetuses with autoimmune-associated congenital heart block followed in the PR Interval and Dexamethasone Evaluation (PRIDE) Study. Am J Cardiol 2009;103:1102–1106.
403. Cuneo BF, Lee M, Roberson D, et al. A management strategy for fetal immune-mediated atrioventricular block. J Matern Fetal Neonatal Med 2010; 23:1400–1405.
404. Trucco SM, Jaeggi E, Cuneo B, et al. Use of intravenous gamma globulin and corticosteroids in the treatment of maternal autoantibody-mediated cardiomyopathy. J Am Coll Cardiol 2011;57:715–723.
405. Ho A, Gordon P, Rosenthal E, Simpson J, Miller O, Sharland G. Isolated complete heart block in the fetus. Am J Cardiol 2015;116:142–147.
406. Brooks P. Fetal manifestations of maternal anti-Ro and La antibodies—more than complete heart block. Australas J Ultrasound Med 2015;18:124–128.
407. Mitchell JL, Cuneo BF, Etheridge SP, Horigome H, Weng HY, Benson DW. Fetal heart rate predictors of long QT syndrome. Circulation 2012; 126:2688–2695.
408. Eliasson H, Sonesson SE, Sharland G, et al. Isolated atrioventricular block in the fetus: a retrospective, multinational, multicenter study of 175 patients. Circulation 2011;124:1919–1926.
409. Friedman DM, Llanos C, Izmirly PM, et al. Evaluation of fetuses in a study of intravenous immunoglobulin as preventive therapy for congenital heart block: Results of a multicenter, prospective, open-label clinical trial. Arthritis Rheum 2010;62:1138–1146.
410. Martinez-Sanchez N, Robles-Marhuenda A, Alvarez-Doforno R, et al. The effect of a triple therapy on maternal anti-Ro/SS-A levels associated to fetal cardiac manifestations. Autoimmun Rev 2015;14:423–428.
411. Zhou KY, Hua YM. Autoimmune-associated congenital heart block: A new insight in fetal life. Chin Med J (Engl) 2017;130:2863–2871.
412. Doti PI, Escoda O, Cesar-Díaz S, et al. Congenital heart block related to maternal autoantibodies: descriptive analysis of a series of 18 cases from a single center. Clin Rheumatol 2016;35:351–356.
413. Hofbeck M, Ulmer H, Beinder E, Sieber E, Singer H. Prenatal findings in patients with prolonged QT interval in the neonatal period. Heart 1997;77:198–204.
414. Hamada H, Horigome H, Asaka M, et al. Prenatal diagnosis of long QT syndrome using fetal magnetocardiography. Prenat Diagn 1999;19:677–680.
415. Vrancken SL, van Heijst AF, de Boode WP. Neonatal hemodynamics: From developmental physiology to comprehensive monitoring. Front Pediatr 2018; 6:87.
416. Williams KP, Farquharson DF, Bebbington M, et al. Screening for fetal well-being in a high-risk pregnant population comparing the nonstress test with umbilical artery Doppler velocimetry: a randomized controlled clinical trial. Am J Obstet Gynecol 2003;188:1366–1371.
417. Cuneo BF, Buyon JP. Keeping upbeat to prevent the heartbreak of anti-Ro/SSA pregnancy. Ultrasound Obstet Gynecol 2019;54:7–9.
418. Bravo-Valenzuela NJ, Rocha LA, Machado Nardozza LM, Araujo Junior E. Fetal cardiac arrhythmias: Current evidence. Ann Pediatr Cardiol 2018; 11:148–163.
419. Nicklas RA, Balazs T. Adverse effects of theophylline-beta agonist interactions. J Allergy Clin Immunol 1986;78:806–811.
420. Lamont RF. The pathophysiology of pulmonary oedema with the use of beta-agonists. BJOG 2000;107:439–444.
421. Ishikawa T, Tsuji Y, Makita N. Inherited bradyarrhythmia: A diverse genetic background. J Arrhythm 2016;32:352–358.
422. Friedman DM, Borg M, Rutkovsky L, Buyon JP. Benign fetal bradycardias diagnosed by echocardiography. Am J Perinatol 1995;12:87–90.
423. Seth R, Moss AJ, McNitt S, et al. Long QT syndrome and pregnancy. J Am Coll Cardiol 2007;49:1092–1098.
424. Rodriguez-Manero M, Casado-Arroyo R, Sarkozy A, et al. The clinical significance of pregnancy in Brugada syndrome. Rev Esp Cardiol (Engl Ed) 2014; 67:176–180.
425. Romagano MP, Quinones JN, Ahnert A, Martinez R, Smulian JC. Catecholaminergic polymorphic ventricular tachycardia in pregnancy. Obstet Gynecol 2016;127:735–739.
426. Strand SA, Strasburger JF, Wakai RT. Fetal magnetocardiogram waveform characteristics. Physiol Meas 2019;40:035002.
427. Doyle NM, Monga M, Montgomery B, Dougherty AH. Arrhythmogenic right ventricular cardiomyopathy with implantable cardioverter defibrillator placement in pregnancy. J Matern Fetal Neonatal Med 2005;18:141–144.
428. Tuzcu V, Kilinc OU. Implantable cardioverter defibrillator implantation without using fluoroscopy in a pregnant patient. Pacing Clin Electrophysiol 2012; 35:e265–e266.
429. Cuneo BF, Etheridge SP, Horigome H, et al. Arrhythmia phenotype during fetal life suggests long-QT syndrome genotype: risk stratification of perinatal long-QT syndrome. Circ Arrhythm Electrophysiol 2013;6:946–951.
430. Cuneo BF, Strasburger JF, Yu S, et al. In utero diagnosis of long QT syndrome by magnetocardiography. Circulation 2013;128:2183–2191.
431. Strand S, Strasburger JF, Cuneo BF, Wakai RT. Complex and Novel Arrhythmias Precede Stillbirth in Fetuses With De Novo Long QT Syndrome. Circ Arrhythm Electrophysiol 2020;13:e008082.
432. Moore JP, Gallotti RG, Shannon KM, et al. Genotype Predicts outcomes in fetuses and neonates with severe congenital long QT syndrome. JACC Clin Electrophysiol 2020;6:1561–1570.
433. Krul SP, van der Smagt JJ, van den Berg MP, Sollie KM, Pieper PG, van Spaendonck-Zwarts KY. Systematic review of pregnancy in women with inherited cardiomyopathies. Eur J Heart Fail 2011;13:584–594.
434. Winbo A, Fosdal I, Lindh M, et al. Third trimester fetal heart rate predicts phenotype and mutation burden in the type 1 long QT syndrome. Circ Arrhythm Electrophysiol 2015;8:806–814.
435. Cuneo BF, Strasburger JF, Wakai RT. The natural history of fetal long QT syndrome. J Electrocardiol 2016.
436. Blais BA, Satou G, Sklansky MS, Madnawat H, Moore JP. The diagnosis and management of long QT syndrome based on fetal echocardiography. HeartRhythm Case Rep 2017;3:407–410.
437. Baruteau AE, Kyndt F, Behr ER, et al. SCN5A mutations in 442 neonates and children: genotype-phenotype correlation and identification of higher-risk subgroups. Eur Heart J 2018;39:2879–2887.
438. Skinner JR, Winbo A, Abrams D, Vohra J, Wilde AA. Channelopathies that lead to sudden cardiac death: Clinical and genetic aspects. Heart Lung Circ 2019; 28:22–30.
439. Tester DJ, Ackerman MJ. Sudden infant death syndrome: how significant are the cardiac channelopathies? Cardiovasc Res 2005;67:388–396.
440. Crotti L, Tester DJ, White WM, et al. Long QT syndrome-associated mutations in intrauterine fetal death. JAMA 2013;309:1473–1482.
441. Scalercio L, Vitter J, Elliott CE. Placement of a continuous stellate ganglion block for treatment of refractory ventricular fibrillation in the setting of known prinzmetal angina during pregnancy: A case report. A A Pract 2019; 12:106–108.
442. Bolin EH, Escalona-Vargas D, Daily JA, et al. Magnetocardiographic identification of prolonged fetal corrected QT interval in women receiving treatment for opioid use disorder. J Obstet Gynaecol Res 2019;45:1989–1996.

443. Waddell-Smith KE, Skinner JR, members of the CGCWG. Update on the diagnosis and management of familial long QT syndrome. Heart Lung Circ 2016; 25:769–776.
444. Rashba EJ, Zareba W, Moss AJ, et al. Influence of pregnancy on the risk for cardiac events in patients with hereditary long QT syndrome. LQTS Investigators. Circulation 1998;97:451–456.
445. Khositseth A, Tester DJ, Will ML, Bell CM, Ackerman MJ. Identification of a common genetic substrate underlying postpartum cardiac events in congenital long QT syndrome. Heart Rhythm 2004;1:60–64.
446. Heradien MJ, Goosen A, Crotti L, et al. Does pregnancy increase cardiac risk for LQT1 patients with the KCNQ1-A341V mutation? J Am Coll Cardiol 2006; 48:1410–1415.
447. Tanaka H, Katsuragi S, Tanaka K, et al. Maternal and neonatal outcomes in labor and at delivery when long QT syndrome is present. J Matern Fetal Neonatal Med 2016;29:1117–1119.
448. Ishibashi K, Aiba T, Kamiya C, et al. Arrhythmia risk and beta-blocker therapy in pregnant women with long QT syndrome. Heart 2017;103:1374–1379.
449. Alvarez SGV, Khoo NS, Colen T, et al. The incremental benefit of color tissue doppler in fetal arrhythmia assessment. J Am Soc Echocardiogr 2019;32:145–156.
450. Mazzanti A, Maragna R, Vacanti G, et al. Interplay between genetic substrate, QTc duration, and arrhythmia risk in patients with long QT syndrome. J Am Coll Cardiol 2018;71:1663–1671.
451. Drugs and Lactation Database (LactMed) Nadolol. National Institute of Child Health and Human Development; 2006. Updated February 23. 2021, https://www.ncbi.nlm.nih.gov/books/NBK501157.
452. Owen HJ, Bos JM, Ackerman MJ. Wearable cardioverter defibrillators for patients with long QT syndrome. Int J Cardiol 2018;268:132–136.
453. Goldenberg I, Horr S, Moss AJ, et al. Risk for life-threatening cardiac events in patients with genotype-confirmed long-QT syndrome and normal-range corrected QT intervals. J Am Coll Cardiol 2011;57:51–59.
454. Barsheshet A, Dotsenko O, Goldenberg I. Genotype-specific risk stratification and management of patients with long QT syndrome. Ann Noninvasive Electrocardiol 2013;18:499–509.
455. Roston TM, Jones K, Hawkins NM, et al. Implantable cardioverter-defibrillator use in catecholaminergic polymorphic ventricular tachycardia: A systematic review. Heart Rhythm 2018;15:1791–1799.
456. Chen X, Zhao H, Sun L, Zhu W, Zhang F. Electrocardiogram characteristics and arrhythmic events during fever in patients with fever-induced Brugada syndrome. Cardiology 2020;145:130–135.
457. Ambardekar AV, Lewkowiez L, Krantz MJ. Mastitis unmasks Brugada syndrome. Int J Cardiol 2009;132:e94–96.
458. Michowitz Y, Milman A, Sarquella-Brugada G, et al. Fever-related arrhythmic events in the multicenter Survey on Arrhythmic Events in Brugada Syndrome. Heart Rhythm 2018;15:1394–1401.
459. Yuan M, Tian C, Li X, et al. Gender differences in prognosis and risk stratification of Brugada syndrome: A pooled analysis of 4,140 patients from 24 clinical trials. Front Physiol 2018;9:1127.
460. Li X, Sacher F, Kusano KF, et al. Pooled analysis of risk stratification of spontaneous type 1 Brugada ECG: focus on the influence of gender and EPS. Front Physiol 2018;9:1951.
461. Vohra J, Rajagopalan S, Group CGCW. Update on the Diagnosis and Management of Brugada Syndrome. Heart Lung Circ 2015;24: 1141–1148.
462. Sharif-Kazemi MB, Emkanjoo Z, Tavoosi A, et al. Electrical storm in Brugada syndrome during pregnancy. Pacing Clin Electrophysiol 2011; 34:e18–e21.
463. Cheung CC, Lieve KV, Roston TM, et al. Pregnancy in catecholaminergic polymorphic ventricular tachycardia. JACC Clin Electrophysiol 2019; 5:387–394.
464. Pflaumer A, Davis AM. An update on the diagnosis and management of catecholaminergic polymorphic ventricular tachycardia. Heart Lung Circ 2019; 28:366–369.
465. Hayashi M, Denjoy I, Extramiana F, et al. Incidence and risk factors of arrhythmic events in catecholaminergic polymorphic ventricular tachycardia. Circulation 2009;119:2426–2434.
466. Imberti JF, Underwood K, Mazzanti A, Priori SG. Clinical Challenges in Catecholaminergic Polymorphic Ventricular Tachycardia. Heart Lung Circ 2016; 25:777–783.
467. van der Werf C, Zwinderman AH, Wilde AA. Therapeutic approach for patients with catecholaminergic polymorphic ventricular tachycardia: state of the art and future developments. Europace 2012;14:175–183.
468. Chow T, Galvin J, McGovern B. Antiarrhythmic drug therapy in pregnancy and lactation. Am J Cardiol 1998;82:58i–62i.
469. Rudic B, Schimpf R, Borggrefe M. Short QT syndrome—review of diagnosis and treatment. Arrhythm Electrophysiol Rev 2014;3:76–79.
470. Hong K, Piper DR, Diaz-Valdecantos A, et al. De novo KCNQ1 mutation responsible for atrial fibrillation and short QT syndrome in utero. Cardiovasc Res 2005;68:433–440.
471. Serra V, Bellver J, Moulden M, Redman CW. Computerized analysis of normal fetal heart rate pattern throughout gestation. Ultrasound Obstet Gynecol 2009; 34:74–79.
472. Doshi AN, Mass P, Cleary KR, et al. Feasibility of non-invasive fetal electrocardiographic interval measurement in the outpatient clinical setting. Pediatr Cardiol 2019;40:1175–1182.
473. Strand S, Lutter W, Strasburger JF, Shah V, Baffa O, Wakai RT. Low-cost fetal magnetocardiography: A comparison of superconducting quantum interference device and optically pumped magnetometers. J Am Heart Assoc 2019; 8:e013436.
474. Fouron JC, McNeal-Davidson A, Abadir S, et al. Prenatal diagnosis and prognosis of accelerated idioventricular rhythm. Ultrasound Obstet Gynecol 2017; 50:624–631.
475. Greutmann M, Silversides CK. The ROPAC registry: a multicentre collaboration on pregnancy outcomes in women with heart disease. Eur Heart J 2013; 34:634–635.

Appendix 1 Writing committee member disclosure of relationships with industry and other entities

Writing committee member	Employment	Honoraria/ Speaking/ Consulting	Speakers' bureau	Research*	Fellowship support*	Ownership/ Partnership/ Principal/ Majority stockholder	Stock or stock options	Intellectual property/ Royalties	Other
José A. Joglar, MD, FHRS (Chair)	The University of Texas Southwestern Medical Center, Dallas, Texas	None	None	None	None	None	None	None	None
Suraj Kapa, MD, FHRS (Vice-Chair)	Mayo Clinic, Rochester, Minnesota	0: Myant Canada 1: Biosig Technologies 1: Philips	1: Abbott	3: Abbott 3: Boston Scientific 3: Toray Industries Inc. 4: Aegis Medical	None	None	None	None	None
Elizabeth V. Saarel, MD, FHRS, CEPS-P (Vice-Chair)	St. Luke's Health System, Boise, Idaho, and Cleveland Clinic Lerner College of Medicine at Case Western Reserve University, Cleveland, Ohio	None	None	None	None	None	None	None	None
Anne M. Dubin, MD, FHRS, CEPS-P	Stanford University, Palo Alto, California	1: Guidepoint Global Advisors	None	None	None	None	None	1: Elsevier 1: UpToDate	None
Bulent Gorenek, MD, FACC	Eskişehir Osmangazi University, Eskişehir, Turkey	1: Bayer Healthcare Pharmaceuticals 1: Daiichi 1: Pfizer, Inc.	None	None	None	None	None	None	None
Afshan B. Hameed, MD, FACOG, FACC	University of California, Irvine, Irvine, California	None	None	None	None	None	None	None	None
Sissy Lara de Melo, MD, PhD	University of São Paulo, São Paulo, Brazil	None	None	None	None	None	None	None	None
Miguel A. Leal, MD, FHRS	University of Wisconsin–Madison, Madison, Wisconsin	None	None	None	1: Medtronic 1: Philips	None	None	None	None
Blandine Mondésert, MD	Montréal Heart Institute, Montréal, Quebec, Canada	2: Abbott Vascular 2: Cook Medical, Inc. 2: Medtronic 2: Boston Scientific	None	5: Boston Scientific	None	None	None	None	None

Luis D. Pacheco, MD	The University of Texas Medical Branch at Galveston, Galveston, Texas	None	None	None	None	None	None	None	None
Melissa R. Robinson, MD, FHRS, CCDS	University of Washington, Seattle, Washington	1: Abbott 1: Biosense Webster, Inc. 1: Biotronik	None	0: Abbott 0: Medtronic	None	None	None	None	None
Andrea Sarkozy, MD, PhD, FEHRA	University Hospital of Antwerp, University of Antwerp, Antwerp, Belgium	1: Biosense Webster, Inc. 1: Biotronik	None	None	None	None	None	None	0:European Heart Rhythm Association
Candice K. Silversides, MD, FRCPC, FACC	University of Toronto, Toronto, Ontario, Canada	None	None	None	None	None	None	None	None
Danna Spears, MD	University Health Network, Toronto, Ontario, Canada	None	None	None	None	None	None	None	None
Sindhu K. Srinivas, MD, MSCE	University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania	None	None	None	None	None	None	None	0: Babyscripts
Janette F. Strasburger, MD	Children's Hospital of Wisconsin, Milwaukee, Wisconsin	None	None	4: National Institutes of Health 2: Scholl Foundation	None	None	None	None	None
Usha B. Tedrow, MD, MS, FHRS	Brigham and Women's Hospital, Boston, Massachusetts	1: Biosense Webster, Inc. 1: Medtronic 1: Abbott 1: Thermedical	None	None	None	None	None	None	None
Jennifer M. Wright, MD, MA, FHRS	University of Wisconsin–Madison, Madison, Wisconsin	None	None	None	None	None	None	None	None

(*Continued*)

Appendix 1 Writing committee member disclosure of relationships with industry and other entities (*Continued*)

Writing committee member	Employment	Honoraria/ Speaking/ Consulting	Speakers' bureau	Research*	Fellowship support*	Ownership/ Partnership/ Principal/ Majority stockholder	Stock or stock options	Intellectual property/ Royalties	Other
Carolyn M. Zelop, MD, FAHA	The Valley Health System, Ridgewood, New Jersey, and New York University Grossman School of Medicine, New York, New York	None	None	None	None	None	None	None	None
Dominica Zentner, MBBS (Hons), FRACP, PhD	The University of Melbourne, Melbourne, Victoria, Australia	None	None	None	None	None	None	None	0: Johnson & Johnson

Number value: **0** = $0; **1** = ≤ $10,000; **2** = > $10,000 to ≤ $25,000; **3** = > $25,000 to ≤ $50,000; **4** = > $50,000 to ≤ $100,000; **5** = > $100,000.

This table is a comprehensive list of the relationships with industry and other entities (RWI)—regardless of relevance to the document topic—disclosed by each writing committee member for the 12 months prior to the initial meeting of the writing committee and up through the completion of the document. The table does not necessarily reflect the RWI of the writing committee members at the time of publication. Please refer to the *HRS Code of Ethics and Professionalism* for definitions of disclosure categories or additional information about the HRS policy on the disclosure of relationships with industry and other entities. To mitigate potential bias and conflict of interest, the recommendations and supportive text were written by writing committee members who were free of relevant RWI.

*Research and fellowship support are classed as programmatic support. Sources of programmatic support are disclosed but are not regarded as a relevant relationship with industry for writing committee members.

Appendix 2 Reviewer disclosure of relationships with industry and other entities

Peer reviewer	Employment	Honoraria/ Speaking/ Consulting	Speakers' bureau	Research*	Fellowship support*	Ownership/ Partnership/ Principal/ Majority stockholder	Stock or stock options	Intellectual property/ Royalties	Other
Elena Arbelo, MD, MSci, PhD	Hospital Clinic de Barcelona and Institut d'Investigació August Pi i Sunyer (IDIBAPS), Barcelona, Spain; Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Madrid, Spain; European Reference Network for rare, low prevalence and complex diseases of the heart (ERN GUARD)	1: Biosense Webster, Inc.	None	None	None	None	None	None	0: European Heart Rhythm Association 0: European Society of Cardiology
Carina Blomström-Lundqvist, MD, PhD	Örebro University, Örebro, Sweden	1: Bayer Healthcare Pharmaceuticals 1: Boston Scientific 1: Cathprint 1: Medtronic 1: Bakken Research Center 1: Merck 1: Philips 1: Sanofi	None	1: Cardiome Pharma/Astellas	None	None	None	None	None
Barbara J. Deal, MD, MS	Northwestern University Feinberg School of Medicine, Chicago, Illinois	None	None	None	None	None	None	None	None
M. Cecilia Gonzalez Corcia, PhD, CEPS-P	Centre Hospitalier Universitaire Sainte-Justine, Montréal, Quebec, Canada	None	None	None	None	None	None	None	None
Rajesh Kabra, MD, FHRS	Kansas City Heart Rhythm Institute, Overland Park, Kansas	None	None	None	None	None	None	None	None

(*Continued*)

Appendix 2 Reviewer disclosure of relationships with industry and other entities (*Continued*)

Peer reviewer	Employment	Honoraria/ Speaking/ Consulting	Speakers' bureau	Research*	Fellowship support*	Ownership/ Partnership/ Principal/ Majority stockholder	Stock or stock options	Intellectual property/ Royalties	Other
Magdalena J. Lagamayo, MD	Philippine Heart Center, Quezon City, Philippines	None	None	None	None	None	None	None	None
Torri Metz, MD	University of Utah Health, Salt Lake City, Utah	None	None	0: GestVision 0: Pfizer	None	None	None	0: UpToDate	None
Sarah Obican, MD	University of South Florida, Tampa, Florida	None	None	None	None	None	None	None	None
Alejandro Olaya, MD	Hospital de San Jose Fundacion Universitaria de Ciencias de la Salud, Bogotá, Colombia	None	None	None	None	None	None	None	1: Abbott 1: Medtronic
Nisha Parikh, MD, MPH	University of California, San Francisco, San Francisco, California	None	None	None	None	None	None	None	None
Andrea M. Russo, MD, FHRS	Cooper University Hospital, Camden, New Jersey	1: Abbott 1: AtriCure, Inc. 1: Bayer Healthcare Pharmaceuticals 1: Biosense Webster, Inc. 1: Biotronik 1: BMS/Pfizer Alliance 1: Boston Scientific 1: Medtronic 1: PaceMate 1: Sanofi	None	1: Kestra 1: MediLynx 1: Medtronic 2: Boston Scientific	1: Medtronic	None	None	1: UpToDate	1: American Board of Internal Medicine
Kamala P. Tamirisa, MD, FHRS	Texas Cardiac Arrhythmia, Dallas, Texas	0: Abbott 1: Medscape	None	None	None	None	None	None	None

Number value: **0** = $0; **1** = ≤ $10,000; **2** = > $10,000 to ≤ $25,000; **3** = > $25,000 to ≤ $50,000; **4** = > $50,000 to ≤ $100,000; **5** = > $100,000.

This table is a comprehensive list of the relationships with industry and other entities (RWI)—regardless of relevance to the document topic—disclosed by the reviewers at the time the document was under review. The table does not necessarily reflect the RWI of the reviewers at the time of publication. Please refer to the *HRS Code of Ethics and Professionalism* for definitions of disclosure categories or additional information about the HRS policy on the disclosure of relationships with industry and other entities.

*Research and fellowship support are classed as programmatic support. Sources of programmatic support are disclosed but are not regarded as a relevant relationship with industry for writing group members or reviewers.