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INTRODUCTION

Cardiac arrhythmias are among the leading cardiac complications in pregnancy.⁽¹⁻³⁾ Cardiac arrhythmias may present for the first time in pregnancy, or present with increasing frequency during pregnancy especially in patients with pre-existing cardiac disease, advanced maternal age or in those with congenital heart defects.⁽³⁻⁶⁾ Furthermore, the presence of arrhythmias in pregnancy portends worse maternal and foetal outcomes.⁽⁷⁾

EPIDEMIOLOGY

The number of pregnancy-related admissions due to arrhythmias have increased over time, this is mostly related to the increase in atrial fibrillation and ventricular tachycardia related hospitalisations in pregnancy.⁽⁶⁾ In a large US nationwide descriptive observational study analysing temporal trends of the frequency and outcomes of arrhythmias in pregnancy related hospitalisations, arrhythmia-related hospitalisations increased from 55/100 000 in 2000 - 83/100 000 in 2012,⁽⁶⁾ mainly due to an increase in AF and VT related admissions which increased by 111% and 127% respectively.⁽⁶⁾ Increasing maternal age and associated comorbidities like hypertension and diabetes mellitus are possible reasons for this increase. For example, Vaidya and colleagues reported an arrhythmia frequency of 199/100 000 (which included sinus tachycardia) in women age between 41 and 50 years compared to only 55/100 000 in those age between 18 - 30 years of age.⁽⁶⁾ The reported frequency of dif-

ABSTRACT

Cardiac arrhythmias are common in pregnancy. The approach to the diagnosis of arrhythmias in pregnancy requires a detailed clinical history and examination and documentation of the arrhythmia preferably on a Holter or electrocardiogram. Treatment of arrhythmias is arrhythmia specific and may require antiarrhythmic drug therapy. However, the risks and benefits of antiarrhythmic drugs must be carefully considered. Catheter ablation remains a treatment option but is seldom required during pregnancy. SAHeart 2022;19:174-180

ferent arrhythmias in pregnancy from 2 cohorts is presented in Table I.

MECHANISMS

The exact mechanisms by which pregnancy increases arrhythmias are unclear. The haemodynamic adaptations of pregnancy, hormonal and autonomic tone alterations has been implicated. Haemodynamic changes include heart rate increases by 20% - 25%, blood volume increases by up to 45% and cardiac output increases by up to 30% - 45%.^(9,10) The increase in blood volume leads to stretching of atrial and ventricular myocytes which can result in early afterdepolarisations, shortened refractory periods, slow conduction, and increased heterogeneity of refractoriness through activation of stretch activated ion channels.^(11,12) For

TABLE I: Reported frequencies of different arrhythmias in pregnancy.

	n = 136 42 Single centre 1992 - 2000 ⁽⁸⁾	n = 57 315 593 >1 200 US hospitals 2000 - 2012 ⁽⁶⁾
	Frequency per 100 000	Frequency per 100 000
Atrial fibrillation (AF)	3	27
Atrial flutter (AFL)	1	4
PACs, PVCs	33	N/A
Sinus tachycardia/bradycardia	104	N/A
Supraventricular tachycardia (SVT)	24	22
Ventricular fibrillation (VF)	1	2
Ventricular tachycardia (VT)	1	16

example, in an isolated rabbit heart model, gradual increases in the right atrial volume and pressure lead to a reduction in right atrial effective refractory periods and increase in inducibility of atrial fibrillation.⁽¹³⁾ These changes were completely reversible with normalisation of right atrial volume and pressure.⁽¹³⁾

Hormonal changes in pregnancy may also play a role arrhythmogenesis associated with pregnancy. For example, Odening and colleagues have recently showed the proarrhythmic effect of Estradiol by demonstrating an increased incidence of polymorphic ventricular tachycardias and premature ventricular tachycardias in Estradiol treated ovariectomised rabbits.⁽¹⁴⁾

GENERAL APPROACH TO A PREGNANT WOMAN WITH PALPITATIONS

Symptoms suggestive of cardiac arrhythmias like palpitations, dizziness, or syncope are common in pregnancy. However, only 10% of the symptomatic episodes correlate with the presence of an arrhythmia on Holter monitoring.⁽¹⁵⁾ In addition, the prevalence of cardiac arrhythmias recorded by ambulatory Holter monitoring is similar in symptomatic and asymptomatic pregnant women.⁽¹⁵⁾ Therefore, our approach to palpitations in pregnancy generally follows that of non-pregnant patients. Obtaining a detailed history and performing a thorough clinical exam is mandatory. Cardiac imaging (echocardiography) is often needed to confirm/exclude structural heart disease. Because palpitations are so common in pregnancy, the clinician should focus on the characteristics of the palpitations and any associated diseases (e.g. hyperthyroidism, infections, and pulmonary embolism). "Palpitations" concerning for an arrhythmia include very rapid (>150bpm) palpitations or a feeling of "skipped beats". An abrupt onset/offset, irregular nature, associated symptoms like pre-syncope or syncope and a family history of cardiac disease/sudden death should alert the clinician of a possible arrhythmia. Palpitations with concomitant structural heart disease (e.g. rheumatic heart disease, congenital heart disease) should not be assumed to be sinus tachycardia. Paroxysmal arrhythmias may be difficult to record and may require a 24 - 48 hour Holter (if occurs daily) or a 5 day Holter (if occurs weekly) or even the implantation of an implantable loop recorder (if episodes are infrequent) especially when more serious arrhythmias are suspected (like AV block, ventricular tachycardia or atrial fibrillation).

TREATMENT

The treatment of arrhythmias in pregnancy should be based on the risk/benefit assessment with particular attention paid to the presence of symptoms, haemodynamic status during the

arrhythmia and the risks to the mother or the foetus posed by the considered treatment strategy. Treatment is generally indicated if an arrhythmia causes significant symptoms, heart failure or left ventricular dysfunction.

Anti-arrhythmic drugs

There are limited randomised controlled trials on the use of anti-arrhythmic drugs in pregnancy and therefore limited data on efficacy and safety of these drugs in pregnancy.⁽¹⁶⁾ The major concern with drug prescription in pregnancy is the potential teratogenic effect of the drug. In 1979 the US Food and Drug Association (FDA) introduced the ABCDX alphabetic categories to designate safety of drug use during pregnancy.^(17,18) Generally, drugs classified as category A were safe to use in pregnancy and those classified as X were contraindicated. However, because of the ambiguity in drugs classified as B, C, and D, in 2015 the US FDA introduced a narrative Pregnancy and Lactation Labelling Rule (PLLR) to guide clinician with the use of drugs during pregnancy, lactation and in men and women of reproductive age.^(17,18) Table II presents the commonly available anti-arrhythmics and their classification. It is important to note that none of the anti-arrhythmic drugs are totally safe (category A) in pregnancy with Sotalol (category B) having the least side-effect profile. Therefore, the potential risks and benefits must be considered before prescribing any of these potentially teratogenic drugs to the mother and foetus.

Direct current cardioversion

Direct current cardioversion is indicated to urgently terminate haemodynamically compromising cardiac arrhythmias, particularly when refractory to pharmacological and non-pharmacological interventions.^(20, 21) Direct current cardioversion in pregnancy is safe with minimal perturbation in foetal haemodynamics as measured by foetal heart rate and umbilical cord blood flow in all trimesters of pregnancy.⁽²²⁾ The risk of inducing pre-term labour with direct current cardioversion is small.⁽¹⁹⁾

Catheter ablation

Ideally catheter ablation should be performed in the non-pregnant patient before conception to treat symptomatic pre-existing arrhythmias. Catheter ablation during pregnancy should be reserved for the rare arrhythmia that is refractory to medical therapy because of the potential risks of ionising radiation to the foetus. Zero fluoroscopy (zero radiation) catheter ablation procedures can be considered in patients with drug refractory cardiac arrhythmias or poorly tolerated recurrent cardiac arrhythmias during pregnancy.⁽²⁰⁾ Such cases should be referred to experienced centres with access to and expertise in the use

TABLE II: Classification of commonly prescribed and readily available anti-arrhythmic drugs.^(16,17,19)

Drug	Vaughan Williams classification	ABCDX FDA classification	Placental Permeable	Transfer to breast milk	Pre-clinical/Clinical
Adenosine	-	C	No	No	No foetal adverse effects reported (limited human data).
Amiodarone	III	D	Yes	Yes	Hypothyroidism, hyperthyroidism, goiter, bradycardia, premature birth, and growth restriction.
Atenolol	II	D	Yes	Yes	Hypospadias (first trimester), birth defects, low birth weight, bradycardia and hypoglycaemia in foetus (second and third trimesters).
Carvedilol	II	C	Yes (No human data)	Yes (No human data)	No adequate human data • bradycardia and hypoglycaemia in foetus • use only if potential benefit outweighs potential risk.
Digoxin	Cardiac glycoside	C	Yes	Yes, breast feeding is possible	Serum levels are unreliable, safe.
Disopyramide	IA	C	Yes	Yes, breast feeding is possible	Uterine contractions • use only when benefit outweighs risk.
Flecainide	IC	C	Yes	Yes, breast feeding is possible	Inadequate human data.
Ivabradine	I-channel Blocker	-	Yes (in animal studies)	Yes (in animal studies)	Inadequate human data. Contraindicated.
Labetalol	II	C	Yes	Yes, breast feeding is possible	No human data.
Metoprolol	II	C	Yes	Yes, breast feeding is possible	Bradycardia and hypoglycaemia in foetus.
Sotalol	III	B	Yes	Yes, breast feeding is possible	Bradycardia and hypoglycaemia.
Verapamil	IV	C	Yes	Yes, breast feeding is possible	Oral verapamil is well tolerated. Use of intravenous verapamil associated with a greater risk of hypotension and subsequent placental hypoperfusion.
Warfarin	Vitamin k antagonist	D	Yes	Yes	Warfarin embryopathy and bleeding

of 3-dimensional mapping systems and intracardiac ultrasound. If fluoroscopy cannot be entirely avoided, catheter ablation should be deferred to the second trimester of pregnancy and abdominal shielding should be performed routinely during the procedure.^(16,20,23) Some arrhythmias like supraventricular tachycardias may completely disappear in the peripartum period and a conservative strategy can be followed.

Implantable cardioverter defibrillator and pacemaker implantation

The most important concern with pacemaker or implantable cardioverter defibrillator implantation in pregnancy is radiation exposure to the foetus. For women with asymptomatic complete heart block with a narrow junctional escape diagnosed during pregnancy (congenital complete heart block is most likely) and pacemaker implantation can be deferred to after delivery.⁽¹⁹⁾ However, permanent pacemaker implantation during pregnancy should be considered in symptomatic complete

heart block especially in those with a wide ventricular escape which can be unstable.⁽¹⁹⁾ When permanent pacemaker or ICD implantation is indicated, general measures to limit foetal radiation exposure must be followed using abdominal shielding with minimal fluoroscopy.

Specific arrhythmia management

Premature atrial complexes

Premature atrial complexes (PACs) are very common in pregnant women with and without cardiovascular symptoms. For example, in a study of 110 consecutive pregnant women with symptoms of palpitations, dizziness, and syncope (study group) and 55 asymptomatic pregnant women (control group); PACs were detected in 56% of the study group and in 58% of the control group by Holter monitoring.⁽¹⁵⁾ Furthermore, only 7% of the study population and 4% of the control had 100 or more PACs during the monitoring period.⁽¹⁵⁾ The management of

PACs is usually conservative, avoidance of potential provoking factors like caffeine, alcohol, and cigarettes.⁽¹⁶⁾ A cardio-selective beta blocker like metoprolol should be considered in very symptomatic patients, preferably not in the first trimester.^(16,24) Although atenolol is readily available in some parts of Africa, its use in pregnancy has been reportedly associated with intrauterine foetal growth restriction and therefore should be avoided.^(17,19)

Paroxysmal supraventricular tachycardia

Paroxysmal supraventricular tachycardias (SVT) encompass a variety of arrhythmias with an atrial or ventricular rate of >100 beats per minute whose mechanism involve the HIS bundle tissue or above.^(23,25) This definition of SVT generally excludes atrial fibrillation. Thus, the SVT conditions include Atrioventricular Nodal Reentrant Tachycardia (AVNRT), Atrioventricular Reentrant Tachycardia (AVRT) and Atrial Tachycardias (AT).^(20,23,25) SVT account for 22 - 24 per 100 000 hospital admissions in pregnant women.^(6,8) In at least 3.9% of patients SVT will present for the first time in pregnancy, however in 22% of women with an established history of SVT, their symptoms worsened in pregnancy.⁽²⁶⁾

The clinical presentation of SVTs in pregnancy is similar to that in non-pregnant state. SVTs characteristically present with palpitations, dizziness, dyspnea, presyncope and infrequently, syncope.^(20,23) The initial evaluation should include a medical history, clinical examination, and an electrocardiogram. Our electrocardiographic approach to tachycardias is presented in Table III.

In patients presenting with haemodynamically stable SVT, vagal manoeuvres (carotid sinus massage or Valsalva) should be attempted first, followed by adenosine 6mg - 18mg (smaller doses should be tried first) if vagal manoeuvres fail to terminate the tachycardia (Figure 1).^(16,19,20,23) Vagal manoeuvres when performed accurately, will terminate SVT in 17% - 41% of patients.^(28,29) However, adenosine will revert SVT to sinus rhythm in more than 90% of patients.^(30,31) Intravenous beta blockers such as metoprolol or propranolol are options (but are not readily available) if adenosine fails to terminate a haemodynamically stable SVT.^(16,20) Direct current cardioversion is the treatment of choice when pharmacological interventions fail to terminate haemodynamically stable SVT or are contraindicated and in patients presenting with haemodynamic instability.^(16,20,23)

For patients presenting with recurrent symptomatic SVT chronic treatment with beta blockers (metoprolol, propranolol) or

calcium channel blockers (verapamil) may be required as initial therapy. In patients who are refractory to beta blockers or calcium-channel blockers, flecainide, propafenone or sotalol may be effective. If possible, these drugs should be avoided in the first trimester and the lowest effective dose must be used.^(16, 23) Flecainide and propafenone should be avoided in those with structural heart disease.⁽³²⁾ Furthermore, calcium-channel blockers and beta blockers should be used with caution in patients with evidence of accessory pathways on a resting ECG or known with AVRT. Catheter ablation is a therapeutic option for very symptomatic and recurrent SVT on medical therapy during pregnancy but is rarely required.^(16,20,23) Zero-fluoroscopy procedure with the use of 3D mapping and intracardiac ultrasound to limit foetal radiation is ideal. Catheter ablation should also be avoided in the first trimester of pregnancy.^(16,20,23)

Atrial fibrillation and atrial flutter

Atrial fibrillation is one of the most common arrhythmias in pregnancy. Atrial fibrillation and atrial flutter are responsible to 27 per 100 000 and 4 per 100 000 hospitalisations in pregnant women respectively. Although AF and AFL can occur in patients with structurally normal hearts, they occur more commonly in patients with structural heart disease.⁽³³⁾ In patients presenting with AF and AFL a thorough clinical exam, ECG, echocardiogram, and laboratory workup to exclude structural heart disease (e.g. rheumatic heart disease) and systemic diseases (e.g. hyperthyroidism) is essential.⁽³³⁾

Acute episodes of AF and AFL causing haemodynamic instability must be treated with direct current cardioversion.^(33,34) Haemodynamically stable patients with AF or AFL of longer than 48 hours or unknown duration, a transesophageal echocardiogram to exclude a left atrial appendage thrombus must be performed or treated with systemic anticoagulation 3 - 4 weeks prior to direct current cardioversion or pharmacological cardioversion and continued for at least 3 - 4 more weeks after cardioversion depending on stroke risk factors.^(33,34) Pharmacological cardioversion can be achieved with flecainide in patient without structural heart disease and must be used in combination with a beta blocker or a non-dihydropyridine calcium channel blocker (ND CCB).^(33,34) Amiodarone must be avoided in pregnancy.⁽¹⁷⁾ If cardioversion is not achieved or is unlikely to be successful, ventricular rate control with beta blockers or non-dihydropyridine CCB with or without digoxin can be introduced.^(33,34)

Atrial fibrillation and flutter are associated with a high risk of stroke and systemic embolism.⁽³³⁾ These could potential get exacerbated by the hypercoagulable state of pregnancy. Sys-

temic anticoagulation should be instituted in those with a high stroke risk as measured by the CHA2DS2VASc score ≥ 2 , the presence of significant mitral stenosis, metallic prosthetic valve, or hypertrophic cardiomyopathy.^(19,33,35) The available anticoagulation options are Warfarin, unfractionated heparin (UFH),

and low molecular weight heparin (LMWH). Anticoagulation in pregnant women has been discussed extensively in recent reviews and is not the focus of the current article.^(19,36,37)

Ventricular arrhythmia

Ventricular tachycardia (VT) and ventricular fibrillation (VF) account for 16 per 100 000 and 2 per 100 000 hospitalisations in pregnancy respectively.⁽⁶⁾ Isolated premature ventricular complexes (PVC) are very common, and a large proportion of women are asymptomatic. In most cases, PVCs are benign, but can occur in patients with underlying structural heart disease.⁽¹⁵⁾ Ventricular arrhythmias in pregnancy are more likely to occur in patients with an established history of prior ventricular arrhythmias and patients with underlying structural heart disease.⁽³⁸⁾

History, physical examination, electrocardiography, and imaging to establish the presence of structural heart disease is essential. Although a wide complex tachycardia is a ventricular tachycardia until proven otherwise, it is important to remember the other differential diagnoses of wide complex tachycardias (Table III). If the QRS morphology during a wide complex tachycardia is

TABLE III: Clinical classification of tachycardias.⁽²⁷⁾

Regular and Narrow QRS Complex	Irregular and Narrow QRS Complex
Sinus tachycardia	Atrial fibrillation
Atrial flutter	Atrial flutter with a variable AV block
AVJRT (AVNRT, AVRT)	Atrial tachycardia with a variable AV block
Atrial tachycardia	Multifocal atrial tachycardia
Regular and Broad QRS Complex	Irregular and Broad QRS Complex
Ventricular tachycardia	Atrial fibrillation with bundle branch block
SVT with bundle branch block	Atrial flutter with a variable AV block + bundle branch block
Paced rhythm	Polymorphic ventricular tachycardia
Antidromic AVRT	
Pre-excited SVT	

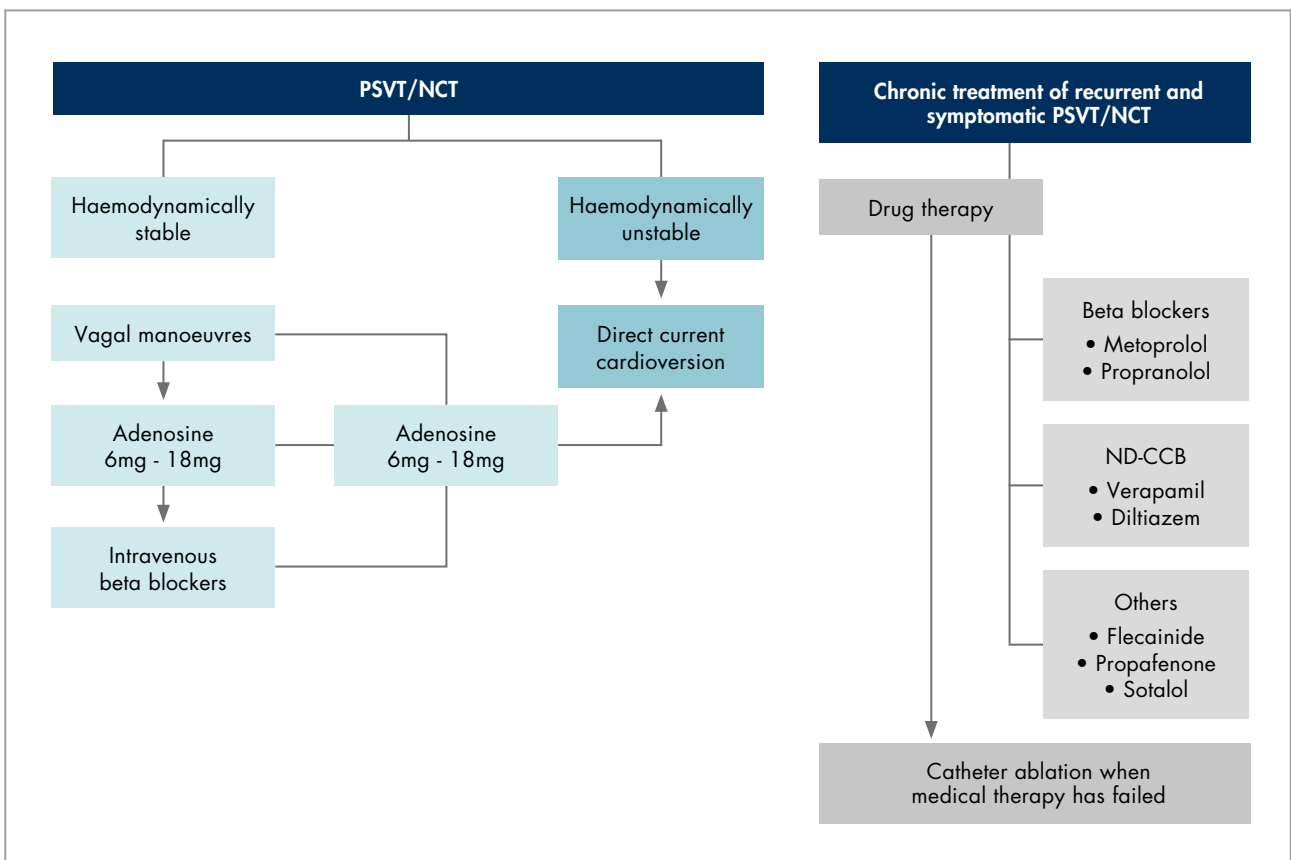


FIGURE 1: Acute treatment of known paroxysmal supraventricular tachycardia or narrow complex tachycardia.

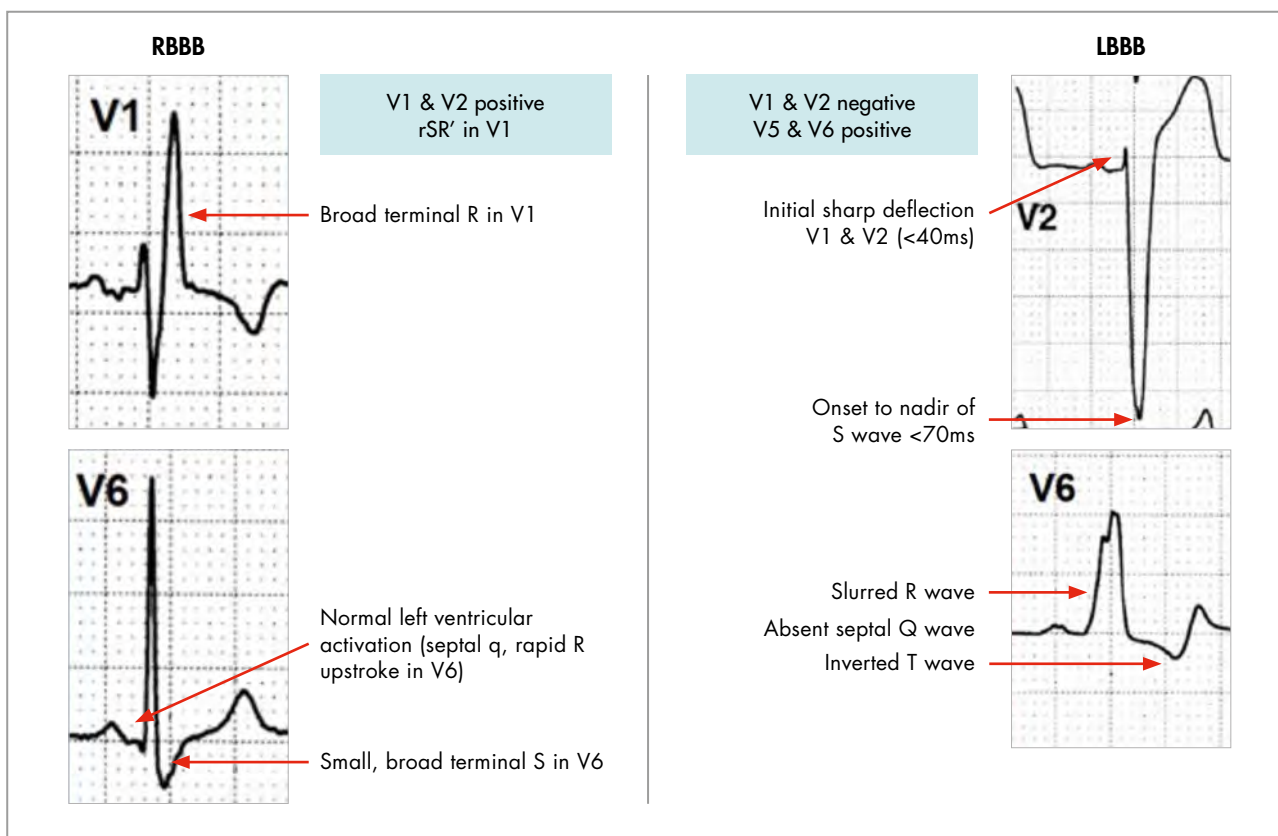


FIGURE 2: Typical bundle branch morphologies for right bundle branch and left bundle branch. A wide complex tachycardia with a QRS morphology not typical for bundle branch block is a ventricular tachycardia until proved otherwise and should be treated as a VT.

not typical for a bundle branch block morphology, then the arrhythmia is probably a VT (Figure 2). One important caveat is the presence of congenital heart disease such as Ebstein's anomalies or Tetralogy of Fallot, in which case the QRS morphology is non-specific making it difficult to differentiate between VT and SVT with a non-specific conduction abnormality.

Direct current cardioversion should be performed for acute management of VT/VF. The chronic management of pregnant women with ventricular arrhythmias and structural heart disease is dependent on the presence of underlying structural heart disease. Flecainide and propafenone must be avoided in patients with structural heart disease.⁽³²⁾ Beta blockers like metoprolol and propranolol are recommended in pregnant women with structural heart disease and recurrent ventricular arrhythmias.⁽¹⁶⁾ Sotalol can be used to prevent recurrences of VT/VF in selected patients. As discussed above, amiodarone is contraindicated in pregnancy.⁽¹⁷⁾ Patients presenting with unstable ventricular arrhythmias and are at high risk for sudden cardiac death and implantable cardioverter defibrillator (ICD) implantation must

be considered.⁽¹⁶⁾ Fluoroscopy reduction principles during ICD implantation must be observed.

CONCLUSION

Sinus tachycardia and premature atrial and ventricular complexes are the most common arrhythmias in pregnancy. The approach to the diagnosis of arrhythmias in pregnancy is the same as the non-pregnant woman. Treatment of arrhythmias is arrhythmia specific and may require antiarrhythmic drug therapy. However, the risks and benefits of antiarrhythmic drugs must be carefully considered on an individual basis. Catheter ablation remains an option for the treatment of arrhythmias but is seldom required during pregnancy.

Conflict of interest: none declared.

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