Management of atrial fibrillation during pregnancy

escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-17/management-of-atrial-fibrillation-during-pregnancy

Vol. 17, N° 15 - 17 Jul 2019

Dr. Ghada Sayed Youssef

The most common cause of atrial fibrillation (AF) during pregnancy is rheumatic mitral valve disease, which is still endemic in the emerging countries. Treatment of chronic AF during pregnancy is challenging. The tachycardia of untreated AF and the rate-controlling drugs and anticoagulants of treated AF all present considerable risk to the foetus. Early detection and treatment of AF can reduce the risk of thromboembolic events. In case of rapid AF and haemodynamic instability, a direct current (DC) shock can be applied with minimal risk to the mother and the foetus.

Arrhythmias, General

Introduction

Atrial fibrillation (AF) is one of the most common cardiac arrhythmias. Haemodynamic abnormalities and thromboembolic events related to AF result in significant morbidity and mortality [1]. Normal pregnancy is associated with increased plasma volume, increased heart rate and increased cardiac output. The occurrence of rapid AF during pregnancy intensifies the haemodynamic burden over the heart and leads to heart failure. Pregnancy is accompanied by an increased concentration of clotting factors and a decrease in anticoagulant factors, resulting in a hypercoagulable state [2]. Whilst it is a concern that this hypercoagulable state can predispose pregnant women with AF to an elevated risk of thromboembolic complications [3], the extent of this risk is not known.

Incidence

AF is the most common arrhythmia in adults, affecting nearly 0.5-1% of the total population and >8% of patients older than 80 years [4]. According to the 2018 European guidelines, the incidence of AF during pregnancy is 27/100,000 [5].

AF in Western countries

AF is unusual during pregnancy in Western countries and, if it occurs, it is either a benign, lone AF or a haemodynamically significant AF, with or without structural heart disease [6].

In a population-based study performed in California, USA, between 2003 and 2013, there

were 264,730 qualifying pregnancies among which AF was noted in 157 pregnancies (129 women; 61.3 per 100,000 women, or 59.3 per 100,000 pregnancies). The prevalence of AF (per 100,000 women) in white, black, Asian, and Hispanic women was 111.6, 101.7, 45.0, and 34.3, respectively. Older age was associated with higher odds of having AF. The odds of AF episodes were higher during the third trimester compared to the first trimester (odds ratio [OR] 3.2, 95% confidence interval [CI]: 1.5-7.7). Among AF patients, adverse maternal cardiac events were rare. Compared to women without AF, foetal birth weights were similar, but the rate of admission to the neonatal intensive care unit for neonates was higher (10.8 vs. 5.1%, p=0.003) [1].

AF in emerging countries

In areas with a high prevalence of rheumatic heart disease, AF is common, especially in young females of child-bearing age.

The incidence of AF differs according to the type and the severity of valvular affection [7]. Diker et al found AF in 29% of patients with isolated mitral stenosis, in 16% with isolated mitral regurgitation, in 52% in combined mitral stenosis and regurgitation, but in only 1% of patients with aortic valvular disease [8]. Mitral valve disease leads to dilatation of the left atrium, elevated left atrial pressure and myocardial stretch, which in turn results in slow conduction velocities, increased dispersion of refractoriness and increased automaticity, all of which create the milieu for initiating and perpetuating sustained AF [9].

The recent results published by the Registry Of Pregnancy And Cardiac diseases (ROPAC) team [10], which included 390 pregnant women with rheumatic mitral valve disease, showed that the overall prevalence of AF before pregnancy was 6.7%; the prevalence was higher among patients with isolated severe mitral stenosis (7.7%). AF failed to show any prediction for either maternal or foetal adverse outcomes.

Clinical perspectives

AF may be diagnosed during pregnancy in patients with valvular heart disease (VHD), congenital heart diseases (repaired or not), cardiomyopathies and hypertension; however, sometimes AF occurs without a structural heart disease (lone AF).

Diagnosis of AF during pregnancy is easily made by clinical examination and electrocardiogram (ECG).

When compared to patients with mitral valve disease without AF, those with AF are in a higher NYHA class, have more severe left ventricular dysfunction and show greater left atrial enlargement [9].

AF during pregnancy in patients with dilated or hypertrophic cardiomyopathy is considered a highly adverse risk factor for maternal morbidity and mortality [5].

AF is associated with an increased mortality risk [11] (OR 13.13, 95% CI: 7.77-22.21, $p<0.0001$], and a rapid ventricular response can lead to serious haemodynamic consequences for both the mother and the foetus.

Treatment

The management of AF during pregnancy has important implications for both maternal and foetal outcomes. AF management comprises therapies with prognostic impact (anticoagulation and treatment of cardiovascular conditions) and therapies predominantly providing symptomatic benefit (rate control and rhythm control) [12]. The choice between rhythm and rate control depends on the severity of the underlying valve disease, haemodynamic stability and tolerance [5].

Drug treatment of AF

Decisions regarding medication use are often difficult, given that, although foetal exposure to a medication may pose risk, failure to treat AF could lead to significant haemodynamic compromise and, in turn, adverse foetal outcomes [1]. Organogenesis occurs during the first trimester, and the developing foetus is sensitive to the potential teratogenic effects of medications. In the second and third trimesters, medications may have potential effects on foetal growth or lead to foetal arrhythmias [5]. Many commonly used medications in AF, such as warfarin and some beta-blockers, have been shown to increase the risks of adverse foetal outcomes [13].

Rhythm control

Rhythm control should be considered as the preferred treatment strategy during pregnancy [12] to avoid potential foetal harm caused by the side effects of the antiarrhythmic and rate control medication and possible haemodynamic instability related to the tachycardia.

Electrical cardioversion is recommended whenever ongoing AF is haemodynamically unstable or if there is a considerable risk for the mother or the foetus. Immediate electrical cardioversion is also needed for pre-excited AF [12,14]. Electrical cardioversion can be used to restore normal sinus rhythm, with low risk to the mother and the foetus [15]. Cardioversion should generally be preceded by anticoagulation [12].

All commonly used antiarrhythmic drugs cross the placenta. Drugs that can be safely used for pharmacological cardioversion during pregnancy are intravenous flecainide and ibutilide (provided there is absence of structural heart diseases) [5]. Amiodarone causes many

adverse foetal outcomes and therefore should not be used during pregnancy [6]. Oral flecainide, propafenone, or sotalol should be considered to maintain sinus rhythm after cardioversion [14].

Rate control

In the case of a rate control strategy, an oral beta-blocker is recommended, with verapamil or digoxin as second choices when beta-blockers are not tolerated (with foetal monitoring for atrioventricular block) [5].

Anticoagulation

Therapeutic anticoagulation is recommended for patients with paroxysmal or persistent AF for the prevention of ischaemic stroke [5]. The decision about starting oral anticoagulants (OACs) should be based upon the results of CHA2DS2-VASc score (Table 1). In general, patients with stroke risk factors (i.e., CHA2DS2-VASc score of 1 or more for men, and 2 or more for women) are likely to benefit from OACs [12].

Table 1. Clinical risk factors for stroke, transient ischaemic attack, and systemic embolism in the CHA2DS2-VASc score. Reprinted with permission from Kirchhof et al [12]. https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Atrial-Fibrillation-Management

CHA2DS2-VASc risk score	Points
Congestive heart failure Signs/symptoms of heart failure or objective evidence of reduced left ventricular ejection fraction	+1
Hypertension Resting blood pressure >140/90 mmHg, on at least two occasions, or Current antihypertensive medication	+1
Age 75 years or older	+2
Diabetes mellitus Fasting glucose >125 mg/dL (7 mmol/L) or treatment with oral hypoglycaemic agents and/or insulin	+1
Previous stroke, transient ischaemic attack or thromboembolism	+2

Vascular disease Previous myocardial infarction, peripheral arterial disease, or aortic plaque	+1
Age 65-74 years	+1
Sex Category (female)	+1

CHA_2DS_2-VASc = Congestive Heart failure, hypertension, Age ≥75 (doubled), Diabetes, Stroke (doubled), Vascular disease, Age 65–74, and Sex (female).

All anticoagulation regimens carry an increased risk of miscarriage and haemorrhagic complications, including post-partum haemorrhage and retroplacental bleeding leading to premature birth and foetal death [5]. Antiplatelet monotherapy is not recommended for stroke prevention in AF patients regardless of stroke risk [12].

Vitamin K antagonists (VKAs)

VKAs can cross the placenta. Their use in the first trimester results in embryopathy (limb defects, nasal hypoplasia) in 0.6-10% of cases [16]. The embryopathy risk is dose-dependent (0.45-0.9% with low-dose warfarin) [17]. There is a 0.7-2% risk of foetopathy (e.g., ocular and central nervous system abnormalities, intracranial haemorrhage) with VKAs in the second and third trimesters [16].

If a low-dose VKA (i.e., warfarin <5 mg/day, phenprocoumon <3 mg/day, or acenocoumarol <2 mg/day) is enough to reach the target therapeutic international normalised ratio (INR) for AF (INR between 2 and 3), then treatment with VKAs should continue in the first trimester with a low risk of teratogenicity. Otherwise, VKAs should be interrupted between 6 and 12 weeks gestation and be replaced by unfractionated heparin (UFH) or low molecular weight heparin (LMWH). VKAs should be stopped at week 36 and should be substituted with UFH/LMWH till delivery. The problem with VKAs is that they need frequent monitoring with the INR test and their level in the foetal circulation cannot be anticipated.

UFH and LMWH

The preferred agents for anticoagulation for AF during pregnancy are heparin compounds. Neither UFH nor LMWH crosses the placenta and both are considered safe in pregnancy. UFH needs multiple injections per day and frequent monitoring with an activated partial thromboplastin time (aPTT) test. LMWH has a better safety profile, with fewer side effects such as thrombocytopaenia, bleeding and osteoporosis [6]. Substitution of VKA with UFH or LMWH in weeks 6-12 almost eliminates the risk of embryopathy [5].

NOACs

Non-vitamin K oral anticoagulation drugs are prohibited during pregnancy [5].

Delivery

According to the most recent European guidelines, AF is considered a low-risk disease during delivery. Even though pregnant women with AF need to see a cardiologist during their pregnancy, they usually do not need a highly qualified delivery centre. As AF is usually associated with cardiac abnormalities, physicians should take into consideration the recommendations for the associated structural heart diseases [5].

Conclusion

Atrial fibrillation during pregnancy is common in emerging countries with a high prevalence of rheumatic valvular heart diseases. Management of AF requires the use of antiarrhythmic and anticoagulant drugs which may affect foetal wellbeing. Pregnant women with AF need to be assessed by a cardiologist throughout pregnancy and before delivery for the proper choice of drugs and for clinical risk assessment.

References

1. Lee MS, Chen W, Zhang Z, Duan L, Ng A, Spencer HT, Kwan DM, Shen AY. Atrial Fibrillation and Atrial Flutter in Pregnant Women-A Population-Based Study. J Am Heart Assoc. 2016;5:e003182.
2. Franchini M. Haemostasis and pregnancy. Thromb Haemost. 2006;95:401-13.
3. Goland S, Elkayam U. Anticoagulation in pregnancy. Cardiol Clin. 2012;30:395-405.
4. Stellbrink C, Nixdorff U, Hofmann T, Lehmacher W, Daniel WG, Hanrath P, Geller C, Mügge A, Sehnert W, Schmidt-Lucke C, Schmidt-Lucke JA; ACE (Anticoagulation in Cardioversion using Enoxaparin) Study Group. Safety and efficacy of enoxaparin compared with unfractionated heparin and oral anticoagulants for prevention of thromboembolic complications in cardioversion of nonvalvular atrial fibrillation: the Anticoagulation in Cardioversion using Enoxaparin (ACE) trial. Circulation. 2004;109:997-1003.
5. Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, Blomstrom-Lundqvist C, Cifkova R, De Bonis M, Iung B, Johnson MR, Kintscher U, Kranke P, Lang IM, Morais J, Pieper PG, Presbitero P, Price S, Rosano GMC, Seeland U, Simoncini T, Swan L, Warnes CA; ESC Scientific Document Group. 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy. Eur Heart J. 2018;39:3165-241.
6. Cacciotti L, Passaseo I. Management of Atrial Fibrillation in Pregnancy. J Atr Fibrillation. 2010;3:295.
7. Sharma SK, Verma SH. A Clinical Evaluation of Atrial Fibrillation in Rheumatic Heart Disease. J Assoc Physicians India. 2015;63:22-5.

8. Diker E, Aydogdu S, Ozdemir M, Kural T, Polat K, Cehreli S, Erdogan A, Göksel S. Prevalence and predictors of atrial fibrillation in rheumatic valvular heart disease. Am J Cardiol. 1996;77:96-8.
9. Shankar PRB, Roa BH, Jaishankar S, Narasimhan M. Current Perspectives: Rheumatic Atrial Fibrillation. J Atr Fibrillation. 2010;2:222.
10. van Hagen IM, Thorne SA, Taha N, Youssef G, Elnagar A, Gabriel H, ElRakshy Y, Iung B, Johnson MR, Hall R, Roos-Hesselink JW; ROPAC Investigators and EORP Team. Pregnancy Outcomes in Women With Rheumatic Mitral Valve Disease: Results From the Registry of Pregnancy and Cardiac Disease. Circulation. 2018;137:806-16.
11. Vaidya VR, Arora S, Patel N, Badheka AO, Agnihotri K, Billimoria Z, Turakhia MP, Friedman PA, Madhavan M, Kapa S, Noseworthy PA, Cha YM, Gersh B, Asirvatham SJ, Deshmukh AJ. Burden of Arrhythmia in Pregnancy. Circulation. 2017;135:619-21.
12. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella M, Diener HC, Heidbuchel H, Hendriks J, Hindricks G, Manolis AS, Oldgren J, Popescu BA, Schotten U, Van Putte B, Vardas P; ESC Scientific Document Group. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J. 2016;37:2893-962.
13. Yakoob MY, Bateman BT, Ho E, Hernandez-Diaz S, Franklin JM, Goodman JE, Hoban RA. The risk of congenital malformations associated with exposure to beta-blockers early in pregnancy: a meta-analysis. Hypertension. 2013;62:375-81.
14. Katritsis DG, Boriani G, Cosio FG, Hindricks G, Jais P, Josephson ME, Keegan R, Kim YH, Knight BP, Kuck KH, Lane DA, Lip GY, Malmborg H, Oral H, Pappone C, Themistoclakis S, Wood KA, Blomström-Lundqvist C, Gorenek B, Dagres N, Dan GA, Vos MA, Kudaiberdieva G, Crijns H, Roberts-Thomson K, Lin YJ, Vanegas D, Caorsi WR, Cronin E, Rickard J. 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.
15. Tromp CH, Nanne AC, Pernet PJ, Tukkie R, Bolte AC. Electrical cardioversion during pregnancy: safe or not? Neth Heart J. 2011;19:134-6.
16. Xu Z, Fan J, Luo X, Zhang WB, Ma J, Lin YB, Ma SH, Chen X, Wang ZP, Ou JS, Zhang X. Anticoagulation Regimens During Pregnancy in Patients With Mechanical Heart Valves: A Systematic Review and Meta-analysis. Can J Cardiol. 2016;32:1248.
17. Hassouna A, Allam H. Limited dose warfarin throughout pregnancy in patients with mechanical heart valve prosthesis: a meta-analysis. Interact Cardiovasc Thorac Surg. 2014;18:797-806.

Notes to editor

Author:

Ghada Sayed Youssef[1,2], MD

1. Assistant Professor of Cardiology, Kasr Al Ainy Hospitals, Cairo University, Cairo, Egypt;
2. Moderator of high-risk pregnancy unit, Cairo University, Cairo, Egypt.

Address for correspondence:

Dr Ghada Sayed Youssef, Kasr Al Ainy Hospitals, Cardiology Department, Cairo University, Cairo, Egypt

E-mail: ghadayoussef@kasralainy.edu.eg

Tel: (+2) 011 511 889 99

Author disclosures:

The author has no conflicts of interest to declare.

The content of this article reflects the personal opinion of the author/s and is not necessarily the official position of the European Society of Cardiology.