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Original Research

Clinical analysis of atrial fibrillation in pregnant women

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Summary

Objective: To analyze the clinical characteristics and risk factors for the major adverse cardiovascular events (MACEs) of atrial fibrillation (AF) in pregnant women. *Materials and Methods:* A retrospective analysis was performed on 35 pregnant women with AF, who were treated at Beijing Anzhen Hospital, Capital Medical University, from January 2004 to May 2017. All pregnancies were recorded. Chi-squared test analysis was performed to determine the correlation between clinical factors and MACEs. *Results:* There were 11 cases of MACEs (31.4%), including 10 cases of heart failure (HF) and 1 case of cerebral infarction. We found 7 clinical factors with a clear correlation with the occurrence of MACEs during pregnancy: a medical history of heart operation ($P = 0.0011$) and AF before pregnancy ($P = 0.0281$), New York Heart Association (NYHA) class ($P < 0.0001$), a left ventricular ejection fraction (LVEF) $\leq$ 50% ($P = 0.0055$), and a delivery time $<$ 37 weeks ($P = 0.0037$). The AF subtype and delivery mode have no correlation with MACEs. *Conclusion:* AF in pregnant women is dangerous for pregnancy and delivery, multi-disciplinary management of obstetricians, cardiologists, and neonatologists are crucial for these patients throughout pregnancy.

Key words: Atrial fibrillation; Pregnancy; Clinical factors; MACEs.

Introduction

Atrial fibrillation (AF), one of the most common cardiac arrhythmias [1], is rare [2] and a cause for concern among pregnant women because of the dramatic changes in hemodynamics throughout pregnancy and delivery [3]. The most common danger is heart failure [4]. Previous studies have shown that hemodynamic abnormalities and thromboembolic events related to AF result in significant morbidity and mortality [5]. AF in pregnant women is usually associated with preexisting heart disease and is common after cardiac surgery [6]. AF in pregnant women is also associated with increased complications for the mother and fetus, such as heart failure, stroke, and death [7].

The limited available literature regarding AF in pregnant women are primarily case studies, and the current therapy for AF in pregnant women is inadequate [8]. According to the 2016 European Society of Cardiology (ESC) guidelines for the management of AF, pregnant women with AF should be positioned in the left lateral position to improve venous return [9]. There were some recommendations for treatment during pregnancy with drugs such as beta-blockers, verapamil, diltiazem, and digoxin, which should be at the lowest dose and for the shortest time required [10]. Meanwhile, electrical cardioversion can also be performed safely at all stages of pregnancy and is recommended in patients who are hemodynamically unstable to AF, and whenever high for the mother or fetus [11]. At the same time, anticoagulation therapy is recommended in patients at risk of stroke. Dose-adjusted heparin is recommended during the first trimester of pregnancy and in the 2-4 weeks before delivery, both heparin and vitamin K antagonists can be used in the remaining parts of the pregnancy [12].

Therefore, multi-disciplinary management of obstetricians, cardiologists, and neonatologists are required throughout pregnancy and should be provided to pregnant women with AF. Our study is based on clinical data from the largest center of cardiovascular disease in pregnant women in Beijing, China. We aimed to analyze the correlation between clinical characteristics and MACEs, including heart failure and cerebral infarction.

Materials and Methods

Study design

A retrospective study of 35 pregnant women with AF (not including early pregnant women with $<$ 14 weeks gestation) from Anzhen Hospital, Capital Medical University, from January 2004 to May 2017. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Capital Medical University. Written informed consent was obtained from all participants.

The diagnosis of AF requires a medical history, clinical symptoms, and electrocardiogram detection [13]. All AF diagnoses before pregnancy or during pregnancy were identified. All patient treatments were developed by obstetricians and cardiologists. Clinical characteristics collected included age, parity, and New York Heart Association (NYHA) class [14], which depends on the left ventricular ejection fraction (LVEF) measured by echocardio-

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Table 1. — *Classification of pregnant women with AF.*

Subtypes of AF	N (%)
I: Lone atrial fibrillation (LAF)	8 (22.8%)
II: Secondary to structural heart disease	24 (68.6%)
AF in CHD	2
AF in RHD	19
AF in Cardiomyopathy	3
III: No structural heart disease	3 (8.6%)
Hypertension atrial fibrillation	1
Hyperthyroid atrial fibrillation	1
Hypothyroid atrial fibrillation	1

graphy.

General patient information, including disease history (including heart disease, heart operation, and other disease), clinical symptoms, medications and operations, parameters, MACEs (includes heart failure, stroke, thromboembolic events, and cardiac death), pregnancy outcomes, obstetric complications, and the time of delivery were all recorded.

Follow-up

A six-week postpartum follow-up was performed for all patients.

Statistical analysis

All analyses were performed with SPSSv19.0 (SPSS Inc., Chicago, IL, USA). Categorical data are presented as frequencies and percentages, and chi-squared tests were used for comparisons. If there were less than five cases in a group, a Fisher's exact test was used.

Results

Baseline characteristics

Eight cases were lone AF, 27 cases were secondary AF, 24 cases were due to structural heart disease, and 3 others were due other diseases (Table 1). The heart function of most patients did not significantly decline since 68.6% (24/35) of cases were NYHA class I-II and 60% (21/35) had an LEVF $\geq$ 50%, while those with worsened outcome were always combined with heart disease history (22/35, Table 2).

Treatment of AF and prevention of thrombus

Eleven patients underwent cardioversion by medication (6), radiofrequency ablation (4), and consulting oxygen and rest (1). Twenty patients were administered medication to control their heart rate, including the 6 who had taken medication for cardioversion. Of the other cases, 2 were treated with verapamil, 6 with beta-blockers, and 6 patients received digitalis. Seventeen patients at high risk of thrombus received anticoagulation therapy: 6 received warfarin, 8 received low-molecular-weight heparins (LMWHs), and 3 received both treatments. One case had cerebral infarction due to the withdrawal of LMWH.

Table 2. — *Maternal baseline characteristics.*

Characteristics	N (%)
Age (years)	
< 35	29 (82.9%)
≥ 35	6 (17.1%)
Multipara	
Yes	6 (17.1%)
No	29 (82.9%)
NYHA class	
I-II	24 (68.6%)
III-IV	11 (31.4%)
LVEF	
$\leq 40\%$	9 (25.7%)
41-54%	5 (14.3%)
$\geq 55\%$	21 (60.0%)
AF medical history	
Yes	22 (62.9%)
No	13 (37.1%)
Symptom	
Symptomatic AF	24 (68.6%)
Asymptomatic AF	11 (31.4%)
Medical history	
AF	22 (62.9%)
Heart failure	0 (0%)
Hypertension	1 (2.9%)
Cerebral infarction	1 (2.9%)
Operation for heart disease pre-pregnancy	13 (37.1%)

Pregnancy outcomes

Three patients had labor induced before 28 weeks of gestation because of heart failure and 10 had premature deliveries. Twenty-eight patients underwent cesarean section because of heart disease or obstetrical complications (Table 3).

Characteristics of patients who have experienced MACEs

Eleven patients had episodes of MACEs during pregnancy and puerperium, including 10 heart failure and 1 cerebral infarction. Ten patients had structural heart disease and 1 had lone-AF (Table 4). The risk factors included a medical history of heart operation ($P = 0.0011$) or AF before pregnancy ($P = 0.0281$), NYHA class ($P < 0.0001$), LVEF% $\leq$ 50% ($P = 0.0055$), and a delivery time < 37 weeks ($P = 0.0037$) (Table 5).

Discussion

In this study, we summarized the features of pregnancy combined with AF in patients who were at risk for MACEs, as well as the pregnancy outcomes. The patients who had structural heart disease and worsened heart function were more likely to suffer MACE, or even heart failure. Poor pregnancy outcomes were always related to poor heart function.

The many physiologic changes during pregnancy for women are well documented; one of the most important

Table 3. — *Pregnancy outcomes of pregnant women with AF.*

Characteristics	N (%)
Delivery week	
≤ 28	3 (8.6%)
28-32 (32)	3 (8.6%)
32-36 (36)	10 (28.6%)
≥ 37	19 (54.3%)
Delivery mode	
Vaginal	7 (20.0%)
Cesarean section	28 (80.0%)
Obstetrical complication	
PROM	2 (5.7%)
Preeclampsia	4 (11.4%)
GDM	2 (5.7%)
Postpartum hemorrhage	1 (2.9%)
Neonatal outcome	
Birth time	
Full-term	19 (54.3%)
Premature	13 (37.1%)
Medical induced abortion	3 (8.6%)
Birth-weight	
Normal	20 (57.1%)
Low	12 (34.3%)
NA	3 (8.6%)
Neonatal asphyxia	
Yes	5 (14.3%)
No	27 (77.1%)

changes is the increasing demands on the cardiovascular system [15]. Peripheral vasodilation during the late pregnancy period always requires an increased cardiac output, which is accomplished by an obvious increase in ventricular end-diastolic volume and contractility [16]. Due to the increased blood and oxygen demands during pregnancy, a variety of cardiovascular changes may promote disease and be dangerous for the mother and fetus; therefore, pregnant women are at a higher risk for developing comorbidities [17], which increases the likelihood for a recurrence of a previously experienced cardiac arrhythmia [18] or *de novo* arrhythmia [19]. At the same time, the significant hormonal changes also increase the incidence of arrhythmias [20].

While most AF in pregnancy are the result of an underlying cardiac arrhythmia or structural abnormality, some women develop new-onset AF during pregnancy [21]. Their presentation and outcomes have not been previously described [22].

The danger of AF is that it can exacerbate heart failure because of structural cardiac remodeling, activation of neurohormonal mechanisms, and impaired left ventricular function. Some studies show that AF in patients with an LVEF $\geq$ 50% or those with heart failure combined with an LVEF $<$ 40% often suffer from poor prognosis [23].

AF can present as lone AF or in parturient with or without structural heart disease. Treatment of AF during pregnancy should be the same as in non-pregnant women and should avoid harm to fetus [24]. In this study, medications were only used for short term for cardioversion, and radiofrequency ablation was also used and produced good results. No adverse events were the result of medication, but labor was induced due to heart failure, which emphasizes the need for effective therapy in pregnant women with AF.

Owing to the risk of stroke, anticoagulation is recommended in pregnant patients with AF [11]. However, the teratogenic effects of the medication must be considered when selecting the appropriate anticoagulant. LMWHs are a safe substitute, as they do not cross the placenta and are recommended during the first trimester of pregnancy and in the 2-4 weeks before delivery [25]. Vitamin K antagonists (such as warfarin) or heparin can be used in the remaining parts of the pregnancy. Non-vitamin K antagonist oral anticoagulants (NOACs) should be avoided in pregnant women and patients planning for pregnancy [26]. There have been 17 patients who received anticoagulants and only one patient suffered cerebral infarction due to LMWH withdrawal, which proved the safety of anticoagulation during pregnancy.

The characteristics of patients who have experienced MACEs suggest that structural heart disease, LVEF, NYHA class, and medical history of AF and heart surgery may be associated with adverse events, so these patients should be given more attention during their pregnancy for MACE prevention.

Limitations

This study has numerous limitations such as incomplete and biased data. The model of delivery in cases of MACEs in this study were all cesarean section, and all vaginal deliveries did not associate with MACEs. This result is likely to be related to the limited number of cases. In addition, this study did not include cases of artificial abortion during the first trimester.

Conclusion

In conclusion, AF in pregnant women also associated with increased complications for the mother and fetus. For patients of AF secondary to structural heart disease, heart surgery before pregnancy can reduce the incidence of adverse events during pregnancy and improve the prognosis. Once diagnosis was confirmed, patients should be referred to a comprehensive hospital with a cardiac center and obstetrics department as soon as possible. Rate and rhythm control and anticoagulation should be provided after careful evaluation of the mother and fetus. Careful monitoring by multi-disciplinary management of obstetricians, cardiologists, and neonatologists are required throughout pregnancy for pregnant women with AF.

Table 4. — *Characteristics of patients who have experienced MACEs in this study.*

Structural-heart disease	MACEs	NYHA class	LVEF (%)	AF	Heart operation before pregnancy
RHD	HF	I-II	55	Y	Y
Cardiomyopathy (PPCM)	HF	III-IV	20	N	N
RHD	HF	III-IV	48	N	N
RHD	HF	III-IV	40	Y	N
RHD	HF	III-IV	44	N	N
RHD	HF	III-IV	40	N	N
RHD	HF	III-IV	33	N	N
Cardiomyopathy (DCM)	HF	III-IV	40	N	N
Cardiomyopathy (RCM)	Cerebral infarction	III-IV	55	N	N
RHD	HF	III-IV	50	Y	N
No	HF	I-II	50	Y	NA

Note: RHD, rheumatic heart disease; PPCM, peripartum cardiomyopathy; DCM, dilated cardiomyopathy; RCM, restrictive cardiomyopathy; HF, heart failure.

Table 5. — *Comparison of clinical factors between patients with and without Major Adverse Cardiovascular Events (MACEs) during pregnancy and postpartum period.*

Clinical factors	MACEs (n = 11)	No MACEs (n = 26)	*P*-value (Chi-square)
Subtype			0.1443 (3.8723)
I	1 (12.5%)	7 (87.5%)	
II	10 (41.67%)	14 (58.33%)	
III	*0*	*3*	
Medical history of heart operation			0.0011 (10.5926)
After Heart operation	1 (7.69%)	12 (92.31%)	
No Heart operation	9 (81.82%)	2 (18.18%)	
NA	*1*	*10*	
NYHA class			< 0.0001 (18.9001)
I-II	2 (8.33%)	22 (91.6%)	
III-IV	9 (81.82%)	2 (18.18%)	
Medical history of AF			0.0281 (4.8228)
Yes	4 (18.18%)	18 (81.82%)	
No	7 (53.85%)	6 (46.15%)	
LVEF%			0.0055 (7.7215)
≤ 50	7 (63.64%)	4 (36.36%)	
>50	4 (16.67%)	20 (83.33%)	
Delivery time			0.0037 (8.4260)
<37 weeks	9 (56.25%)	7 (43.75%)	
≥ 37week	2 (10.53%)	17 (89.47%)	
Delivery mode			0.1218* (2.3946)
Vaginal	0	7 (100%)	
Cesarean section	11 (39.29%)	17 (60.71%)	

Note: *Pearson's Chi-squared test with Yates' continuity correction.

Conflicts of interest

The authors declare no conflict of interest.

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