

Atrial fibrillation with a structurally normal heart in pregnancy: An international survey on current practice

Annabelle Cumyn¹, Nadine Sauvé¹ and Évelyne Rey²

Abstract

Background: Little evidence exists for the optimal management of atrial fibrillation with a structurally normal heart in pregnancy.

Methods: A survey was sent to members of two associations to obtain input on optimal management of atrial fibrillation in pregnancy. The survey presented four cases with respect to (1) baseline investigations; (2) rate versus rhythm control; (3) chemical versus electrical cardioversion; and (4) anticoagulation.

Results: Sixty-one responders from 11 countries participated. High agreement was noted for baseline investigations. A quarter (25%) of participants chose elective cardioversion even with a reversible precipitant. Electrical cardioversion was preferred over chemical ($p < 0.05$). Anticoagulation strategies were heterogeneous except in the presence of a left atrial appendage thrombus.

Discussion: This study revealed that there was little consensus in current practice in pregnancy beyond basic investigations. An adaptation of established guidelines to the pregnant population would require a meeting of Cardiologists with input from colleagues in Obstetric Medicine.

Keywords

High-risk pregnancy, cardiac, drugs (medication)

Date received: 15 October 2016; accepted: 14 November 2016

Introduction

Pregnancy is associated with several cardiovascular adaptations including increased blood volume resulting in myocardial distension and increased heart rate secondary to increased plasma catecholamine concentrations and adrenergic receptor sensitivity.¹ In addition to these physiologic changes, direct electrophysiological effects of hormones and electrolytic alterations may enhance the risk of dysrhythmia.^{2,3} Common electrocardiographic (ECG) findings include sinus tachycardia and premature ventricular contractions. Non-sustained supraventricular arrhythmias are encountered in 30–50% of pregnant women investigated for palpitations, while sustained arrhythmia is less common at around 2–3/100.^{3–5} A review of hospital admissions for cardiac arrhythmia in pregnancy showed sinus arrhythmia/tachycardia/bradycardia in 60%, premature atrial/ventricular contractions in 19% and supraventricular tachycardia in 14%.⁵ Atrial fibrillation (AF) in the absence of congenital or acquired heart disease is therefore rare and accounted for only 1% of all admissions for arrhythmia in pregnant women, with a prevalence of 2/100,000 pregnancies. Furthermore, the majority of reported cases were secondary to medical causes including medication or drug toxicity, pulmonary embolism, hyperthyroidism, and preeclampsia.⁶

A recent case-series of AF with a structurally normal heart in pregnancy showed that the 16 registry cases followed a benign course with a high rate of spontaneous cardioversion (in 81% of AF episodes).⁷ However, management in both registry and published cases series included cardioversion (electrical or chemical) in one-third of AF episodes and a heterogeneous approach to anticoagulation. Three factors may result in a wide range of practice patterns (a) little exposure to AF in pregnancy; (b) care delivery from a varied group of health professionals, and (c) extrapolation from short case series with the risk of publication bias and the unclear applicability of the non-pregnant literature.

Methods

Survey

In 2013, a web-based survey was created to identify whether a consensus in practice existed among specialists in Obstetric Medicine on

the management of AF with a structurally normal heart in pregnancy with respect to (a) baseline investigations; (b) rate versus rhythm control; (c) chemical versus electrical cardioversion; and (d) anticoagulation. The survey presented four fictional cases matched for baseline characteristics but differing in clinical presentation as detailed in Table 1. Other clinical, laboratory, and radiological data were identical.

Case presentations were divided into three sections (baseline investigations, management and anticoagulation) and were presented in a step-wise approach allowing for three distinct groups of questions. Questions on baseline investigations had to be answered first and subsequent questions were answered after initial results (for e.g. thyroid stimulating hormone (TSH), electrolytes, echocardiogram findings) were provided without the possibility of modifying previous answers based on new information. The cases were also presented sequentially so that, whereas cases A and B were used to identify differences in baseline investigations, case C was added to cases A and B to contrast answers on management, and case D was added for questions on anticoagulation.

For increased validity evidence, the cases and the survey's 25 questions were written by three obstetric internists and peer-reviewed by four experts in Obstetric Medicine and 1 expert in scientific writing. In addition, at the end of the survey, participants were asked to provide their level of agreement with the proposed diagnoses.

¹Department of Medicine, Faculté de Médecine et des Sciences de la santé, Université de Sherbrooke, Sherbrooke, Quebec, Canada

²Department of Obstetrics and Gynecology, Centre Hospitalier Universitaire Sainte Justine, Université de Montréal, Montréal, Canada

Corresponding author:

Annabelle Cumyn, Department of Internal Medicine, 3001, 12^{ème} avenue Nord, Sherbrooke, Quebec J0B 1M0, Canada.

Email: annabelle.cumyn@USherbrooke.ca

Table 1. Clinical features of the four cases of AF in pregnancy.

Case	Unique features	Proposed diagnosis	Included in sections on:
A	Symptoms of profuse diarrhoea Treated with volume replacement Spontaneous cardioversion at 12 h post admission	AF with clear precipitant	Baseline investigations Management Anticoagulation
B	Persistence of AF at 48 h Investigations for pulmonary embolism (negative) Digoxin loading	Persistent AF	Baseline investigations Management Anticoagulation
C	BP 80/40 and AF at 190/min Electrical cardioversion Recurrent symptomatic episodes	Recurrent paroxysmal AF	Management Anticoagulation
D	Asymptomatic 1.2-cm clot found on trans-esophageal echocardiogram	AF of unknown duration and left atrial appendage clot	Anticoagulation

Participants

Potential participants included members of the ObMed ListServ (an international directory created by Michael Carson, M.D. and supported by the North American Society of Obstetric Medicine (NASOM), the International Society of Obstetric Medicine (ISOM) and the Society of Obstetric Medicine of Australia and New Zealand (SOMANZ) for health professionals to exchange on complex cases in pregnancy) and members of the Groupe d'Étude en Médecine Obstétricale du Québec (GÉMOQ, an association of Quebec physicians with an interest in Obstetric Medicine). After ethics review and approval (Centre Hospitalier Universitaire Sainte Justine Research Ethics Board project #3684), an e-mail invitation was sent to all potential participants.

Analyses

Analyses included standard descriptive statistics and calculation of percent agreement and Kappa coefficient as a measure of interrater agreement. A p value < 0.05 was considered statistically significant.

Results

Sample characteristics

A total of 61 respondents completed the survey. Respondents came from 11 different countries with a majority from Canada (62%) followed by United States of America (11%) and the United Kingdom (6%). Seven specialties were represented with a predominance of general internists (40%) and obstetric internists (30%). Cardiologists represented 12% of the sample and obstetrics-gynecologists, 10%.

Although one-third of the sample had greater than 15 years of exposure to medical conditions in pregnancy (MCP), exposure to isolated AF in pregnancy is rare. Only 12% of responders had seen more than 10 cases of AF on a structurally normal heart, whereas 28% had never seen this condition at all. The majority of exposure to AF was more likely to occur in the context of congenital or acquired heart disease with 80% of our respondents having followed more than five pregnancies complicated by congenital or acquired heart disease.

Agreement with case content

A high level of agreement was found between proposed diagnosis and participants' comprehension of the cases in three out of four scenarios as shown in Table 2.

Table 2. Level of agreement with proposed diagnosis.

Case	Proposed diagnosis at the end of survey	% agreement (agree or strongly agree)
A	AF with clear precipitant	95
B	Persistent AF	75
C	Recurrent paroxysmal AF	91
D	AF of unknown duration and left atrial appendage clot	95

We speculate that case B met with a lower level of agreement because the case presentation did not meet the time criterion of seven days associated with the definition of persistent AF.

Initial investigations

Whether the episode of AF was associated with a precipitant (case A) or not (case B), a significant level of consensus (greater than 80% agreement with a Kappa coefficient greater than .70) was obtained for the following initial investigations: complete blood count (CBC), electrolytes including magnesium, creatinine, electrocardiogram (ECG), and trans-thoracic echocardiogram (TTE). No consensus was achieved on other initial investigations including chest radiograph (CXR), TSH, or investigations for pulmonary embolism. When asked to select factors that would modify their approach to initial investigations, 72% selected a past history of AF and a past history of venous thromboembolism. Of note, maternal age, body mass index (BMI), persistence of AF and multiple gestations did not appear to modify initial investigations (kappa coefficient less than 0.50).

Treatment: Rate versus rhythm control

Rate control with beta-blockers was the treatment of choice in the first 48 h in both case A, (selected by 66% for AF associated with a potential precipitant) and case B (selected by 67% for AF persisting at 48 h). Beta-blockers were selected twice as often as calcium channel blockers ($p < 0.01$). Oral digoxin was added by 60% in case B and only 36% in case A ($p < 0.01$).

Despite a preference for rate control, a proportion of participants was inclined to resort to cardioversion whether emergency, elective (but within the same hospital stay), or after four weeks of

Table 3. Percentage of participants having selected each strategy of cardioversion.

	Emergency cardioversion (%)	Elective cardioversion (%)	Cardioversion after four weeks of anticoagulation (%)
Case A: AF with clear precipitant	10	22	8
Case B: Persisting AF	10	25	25
Case C: Recurrent paroxysmal AF with borderline BP	83*	8**	4

Note: Participants were not restricted to a single answer.

* $p < 0.01$ relative to cases A and B.

** $p < 0.05$ relative to cases A and B.

anticoagulation in all three cases, with no significant differences between cases A and B as detailed in Table 3.

For case C, where the presentation was associated with some evidence of hemodynamic instability, emergency cardioversion was selected over immediate rate control (83 vs. 13%). When asked to select factors that would favour cardioversion, hemodynamic instability was selected by 96%, ongoing symptoms by 64%, and recent onset by 62%. Of interest, elevated BMI (greater than 40), a past history of AF or the persistence of AF did not appear to modify the decision (selected by less than 20% of responders).

Cardioversion: Electrical versus chemical

Respondents had a preference for electrical over chemical cardioversion in all situations where cardioversion was considered ($p < 0.05$).

This question was associated with a high number of comments ($N = 30$). Several comments ($N = 11$) suggested that electrical cardioversion was more effective, more predictable, and safer for the fetus. Others stated that both strategies were equally effective and that the decision depended on factors such as trimester, BMI, and the risk of intubation. A few comments ($N = 4$) demonstrated a certain degree of discomfort with either approach: “‘defer to cardiologist’, ‘have no experience with treating women in this condition’”.

Anticoagulation

We note that the questions on anticoagulation were only answered 2/3 of the respondents which may translate a certain level of discomfort with the concept of ‘optimal management’.

In the setting of a clear precipitant

In the setting of AF with a clear precipitant, respondents were equally divided between no therapy and oral aspirin as detailed in Table 4.

Therapeutic anticoagulation. Anticoagulation with therapeutic low-molecular weight heparin (LMWH) was the single most common strategy across three of the four cases (Table 4).

Postpartum anticoagulation. Several respondents chose to pursue aspirin in the postpartum setting: 25% in the setting of AF with a clear precipitant and 34% for persisting AF. In the setting of AF with hemodynamic instability, the most frequent selections included aspirin (27%) and prophylactic dose of LMWH (30%). In the setting of AF with a left atrial appendage clot, there was a general consensus for therapeutic anticoagulation whether with LMWH (50%), vitamin K antagonist (28%), or direct oral anticoagulants (3%).

Table 4. Percentage of all participants selecting different strategies of anticoagulation.

	No therapy (%)	ASA (%)	LMWH
Case A: AF with clear precipitant	41	40	11% prophylactic dose 4% intermediate dose 4% therapeutic dose
Case B: Persisting AF	7	36	16% prophylactic dose 7% intermediate dose 32% therapeutic dose
Case C: Recurrent paroxysmal AF with borderline BP	2	27	21% prophylactic dose 7% intermediate dose 41% therapeutic dose
Case D: AF of unknown duration and left atrial appendage clot	4	4	2% prophylactic dose 2% intermediate dose 82% therapeutic dose

Note: Participants could select a combination of therapies; data on vitamin K antagonists and direct oral anticoagulants (DOACs) excluded from table because rarely selected.

Risk assessment scores. Although traditional risk assessment scores (CHADS₂ and CHA₂DS₂-Vasc) have not been validated in pregnancy, 2/3 of respondents declared having used the risk score – in part or completely, to base their decision on anticoagulation.

Discussion

AF with a structurally normal heart is rare in pregnancy. Much of the literature pertains to arrhythmia in general and often in women with established heart disease,^{3,8–10} as well as to drug options in pregnancy.^{11,12} Established guidelines and their focused updates^{13–20} dedicate brief sections to pregnancy which focus mainly on drug safety and prevention of thromboembolic complications in high-risk women. Little evidence is available to propose which adaptations are necessary in the setting of pregnancy and unprovoked AF with a structurally normal heart. Should these women be investigated for pulmonary embolism even in the absence of symptoms, should CXRs be prescribed routinely? Is sinus rhythm a priority to preserve optimal fetal circulation? Are there situations where chemical cardioversion is preferred to electrical cardioversion? What defines high-risk thromboembolism in pregnancy in this population? To these pregnancy-related questions can be added issues surrounding gender differences in the pathophysiology and response to treatment, an issue beyond the scope of this discussion.^{21–24}

Commonalities and differences between practice and current guidelines

In terms of initial basic investigations, this survey of practice reflects closely the content of guidelines established outside of pregnancy. For the pregnant woman with a first episode of AF, regardless of the cause, this group of physicians prescribed a basic set of investigations including CBC, electrolytes (including magnesium), renal function, TSH, ECG, and TTE.

In contrast to guidelines that seem to put beta-blockers and non-dihydropyridine calcium channel antagonists (CCB) on equal footing,¹⁵ 2/3 participants in this survey selected intravenous or oral beta-blockers for rate control in the presence of rapid AF over CCB (selected by one third of the sample). We suspect that this is because more data on security are available with beta-blockers for pregnant women compared to CCB.²⁵

Whereas rate control (and even lenient rate control) seems to gain favour over rhythm control in specific populations such as patients with heart failure,^{26–28} physicians may presume that sinus rhythm in pregnancy is a more optimal rhythm for fetal circulation, even in the hemodynamically stable patient. Whether guided by considerations of preservation of optimal fetal circulation or the risk of tachycardiomyopathy, a significant percentage of our participants considered different strategies for cardioversion. This is interesting in light of recent data based on review of the literature and registry data, showing a high rate of spontaneous cardioversion.⁷ It is possible, therefore, that clinicians should be more patient in the setting of hemodynamic stability before resorting to rhythm control. With regard to management of AF in pregnancy, guidelines do present clear data on the safety profile of medications, the possibility to pursue electrical or chemical cardioversion but have little evidence to guide the clinician as to when ‘arrhythmia conversion is mandatory’ or ‘Direct current cardioversion considered inappropriate’.¹⁵

The question of anticoagulation presented the most heterogeneity in responses. Variation was found in the prescription of ASA and the indications and dosages of LMWH. Our sample population seemed to favour anticoagulation given the high rates of anti-platelet or anticoagulant prescription across all cases. Whether the well-established increased risk of thromboembolic complications translates in an increased risk of stroke in AF for pregnant patients is unknown although the case report of a pregnant patient with AF of unknown duration and a left atrial appendage clot is a reminder of the possibility of complications.⁷ In other words, to what extent are clinicians correct in viewing pregnancy as a risk factor for stroke in AF? In their review of anticoagulation in pregnancy, Goland and Elkayam²⁹ express the opinion that a short episode of lone AF is not an indication for anticoagulation. The ACC/AHA/ESC 2006 guidelines¹⁴ suggest protection against thromboembolic complications by means of aspirin or anticoagulant therapy for all patients with AF except those with lone AF or low thromboembolic risk. Similar statements can be found in the European Society of Cardiology (ESC) Task Force for the management on AF issued in 2010.¹⁵ These guidelines, however, do not provide details on how to grade thromboembolic risk. It is interesting to note that, given the absence of alternative, participants did resort to calculating traditional risk scores (such as CHADS₂ score), even though they acknowledged their lack of validation in pregnancy.

Limitations

This description of current practice is limited by sample size. This reflects the relatively new discipline of Obstetric Medicine in North America and across the globe. A small proportion of our sample (12%) was represented by cardiologists. The remainder, however, had significant expertise in pregnancy. Input from a greater number of cardiologists, perhaps by means of a conference such as the Cardiac Problems in Pregnancy conference, would increase sample size by

reaching beyond the relatively new and small community of Obstetric Physicians.

No available published tool existed on which to base our survey. We recognize that a step-wise case-based survey methodology is a novel approach to documenting current practice. Steps were taken to validate content, both medical and pedagogical, by review with subject-matter experts. In addition, when participants were asked to provide feedback on the survey methodology for reaching consensus, a certain degree of healthy skepticism was present (22% against and 22% uncertain). Comments included the following reflections: ‘We should need more data.’; ‘I strongly disagree with using a survey to establish guidelines. [...] Since little evidence exists on this particular topic, a high degree of consensus among experts (eg >80%) should be sought if the recommendations are to be of any value.’; ‘The survey is very interesting to establish the practice pattern of physicians but has not undergone rigorous discussions and debate of the existing literature to serve as the basis for guidelines’; and ‘I think this is an excellent start [...]’. We agree wholeheartedly with these opinions. The aim of the survey was to describe current practice to help experts subsequently reflect on current management and create more precise guidelines.

Conclusion

Rare conditions in pregnancy provide considerable challenges to all clinicians involved in the care of these women. Not only must the clinician be aware of the impact of the pathophysiology and the interventions on the pregnancy, but they may have many questions on how to adjust risk assessment and intensity of management. AF is an example of a condition for which much data exist outside of pregnancy but how they can be applied to the pregnant patient is unclear. We cannot stress enough the importance of expert multi-disciplinary involvement in the best care of women with complex medical problems. This approach becomes particularly important in the absence of clear, evidence-based guidelines. Logistic barriers are such that high-level evidence is unlikely to be a source of answers in the near future. We wished to explore whether a survey methodology could contribute by providing data regarding current practice patterns of physicians involved in medical complications of pregnancy. Awaiting more data from large registry or prospective multicenter studies, we can conclude that further guidance and clarification by experts, including cardiologists, are needed with regard to the importance of rhythm control relative to rate control and the assessment of thromboembolic risk in this population. Dissemination of more precise recommendations would greatly help clinicians faced with this uncommon condition to identify the correct degree of intervention. A follow-up survey of practice would help to ensure that adequate knowledge translation took place.

Acknowledgements

We would like to thank all our colleagues who participated in the survey.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Contributorship

AC, ER, and NS designed the study. AC created the cases and the survey. ER and NS reviewed survey content with feedback from subject-matter experts (both in Obstetric Medicine and survey

methodology). AC collected, analysed the data and wrote the paper. ER assisted in the data analysis. ER and NS reviewed the paper.

Ethical approval

Ethical approval was obtained from the Comité d'éthique de la recherche du CHU Sainte Justine (project 3684). Approval was granted on 3 June 3 2013. Consent was obtained from each participant prior to participation in this study.

Guarantor

AC

Previous presentation of data

An oral presentation was given and an abstract included in the Program of the February 2014 Cardiac Problems in Pregnancy Conference in Venice, Italy.

References

- Kron J and Conti JB. Arrhythmias in the pregnant patient: Current concepts in evaluation and management. *J Interv Card Electrophysiol* 2007; 19: 95–107.
- Gowda RM, Punukollu G, Khan IA, et al. Lone atrial fibrillation during pregnancy. *Int J Cardiol* 2003; 88: 123–124.
- Adamson DL and Nelson-Piercy C. Managing palpitations and arrhythmias during pregnancy. *Heart* 2007; 93: 1630–1636.
- Shotan M, Ostrzega M, Mehra M, et al. Incidence of arrhythmias in normal pregnancy and relation to palpitations, dizziness, and syncope. *Am J Cardiol* 1997; 79: 1061–1064.
- Li J, Nguyen C, Joglar JA, et al. 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.
- DiCarlo-Meacham A and Dahlke J. Atrial fibrillation in pregnancy. *Obstet Gynecol* 2011; 117: 489–492.
- Sauvé N, Rey É and Cumyn A. Atrial fibrillation on a structurally normal heart in pregnancy: A case series and review of the literature. *J Obstet Gynaecol Can* 2017; 39: 18e24.
- Gowda RM, Khan IA, Mehta NJ, et al. Cardiac arrhythmias in pregnancy: Clinical and therapeutic considerations. *Int J Cardiol* 2003; 88: 129–133.
- Ferrero S, Colombo BM and Ragni N. Maternal arrhythmias during pregnancy. *Arch Gynecol Obstet* 2004; 269: 244–253.
- Flores JR and Marquez MF. Arrhythmias in pregnancy. How and when to treat? *Arch Cardiol Mex* 2007; 77(Suppl 2): 24–31.
- Joglar JA and Page RL. Treatment of cardiac arrhythmias during pregnancy. *Drug Saf* 1999; 20: 85–94.
- Joglar JA and Page RL. Antiarrhythmic drugs in pregnancy. *Curr Opin Cardiol* 2001; 16: 40–45.
- Klein W, Blomstrom-Lundqvist C, de Backer G, et al. Expert consensus document on management of cardiovascular diseases during pregnancy. *Eur Heart J* 2003; 24: 761–781.
- Fuster V, Rydén LE, Cannom DS, et al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: Full text. *Europace* 2006; 8: 651–745.
- Camm AJ, Kirchhof P, Lip GY, et al. Guidelines for the management of atrial fibrillation The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Eur Heart J* 2010; 31(19): 2369–429.
- Cairns JA, Connolly S, McMurry S, et al. Canadian Cardiovascular Society atrial fibrillation guidelines 2010: Prevention of stroke and systemic thromboembolism in atrial fibrillation and flutter. *Can J Cardiol* 2011; 27: 74–90.
- Gillis AM, Verma A, Talajic M, et al. Canadian Cardiovascular Society atrial fibrillation guidelines 2010: Rate and rhythm management. *Can J Cardiol* 2011; 27: 47–59.
- Camm AJ, Lip GY, De Caterina R, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation. *Eur Heart J* 2012; 33: 2719–2747.
- Skane AC, Healey JS, Cairns JA, et al. Focused 2012 update of the Canadian Cardiovascular Society atrial fibrillation guidelines: Recommendations for stroke prevention and rate/rhythm control. *Can J Cardiol* 2012; 28: 125–136.
- Verma A, Cairns JA, Mitchell LB, et al. 2014 focused update of the Canadian Cardiovascular Society Guidelines for the management of atrial fibrillation. *Can J Cardiol* 2014; 30: 1114–1130.
- Villareal RP, Woodruff AL and Masumi A. Gender and cardiac arrhythmias. *Tex Heart Inst J* 2001; 28: 265.
- Wolbrette D, Naccarelli G, Curtis A, et al. Gender differences in arrhythmias. *Clin Cardiol* 2002; 25: 49–56.
- Yarnoz MJ and Curtis AB. More reasons why men and women are not the same (gender differences in electrophysiology and arrhythmias). *Am J Cardiol* 2008; 101: 1291–1296.
- Volgman AS, Manankil MF, Mookherjee D, et al. Women with atrial fibrillation: greater risk, less attention. *Gen Med* 2009; 6: 419–432.
- 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.
- Allen LaPointe NM, Sun J-L, Kaplan S, et al. Rhythm versus rate control in the contemporary management of atrial fibrillation in-hospital. *Am J Cardiol* 2008; 101: 1134–1141.
- Roy D, Talajic M, Nattel S, et al. Rhythm control versus rate control for atrial fibrillation and heart failure. *N Engl J Med* 2008; 358: 2667–2677.
- Van Gelder IC, Groenveld HF, Crijns HJ, et al. Lenient versus strict rate control in patients with atrial fibrillation. *N Engl J Med* 2010; 362: 1363–1373.
- Goland S and Elkayam U. Anticoagulation in pregnancy. *Cardiol Clin* 2012; 30: 395–405.