Cardiac function and cardiac events 1-year postpartum in women with congenital heart disease

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Background Pregnancy is increasingly common in women with congenital heart disease (CHD), but little is known about long-term cardiovascular outcome after pregnancy in these patients. We studied the incidence of cardiovascular events 1-year postpartum and compared cardiac function prepregnancy and 1-year postpartum in women with CHD.

Methods From our national, prospective multicenter cohort study, 172 women were studied. Follow-up with clinical evaluation and echocardiography and NT-proBNP measurement were performed during pregnancy and 12 months postpartum. *Cardiovascular events* were defined as need for an urgent invasive cardiovascular procedure, heart failure, arrhythmia, thromboembolic events, myocardial infarction, cardiac arrest, cardiac death, endocarditis, and aortic dissection.

Results Cardiovascular events were observed after 11 pregnancies (6.4%). Women with cardiovascular events postpartum had significant higher NT-proBNP values at 20-week gestation (191 [137-288] vs 102.5 [57-167]; $P = .049$) and 1-year postpartum compared with women without cardiovascular events postpartum (306 [129-592] vs 105 [54-187] pg/mL; $P = .014$). Women with cardiovascular events during pregnancy were at higher risk for late cardiovascular events (HR 7.1; 95% CI 2.0-25.3; $P = .003$). In women with cardiovascular events during pregnancy, subpulmonary end-diastolic diameter had significantly increased 1-year postpartum (39.0 [36.0-48.0] to 44.0 [40.0-50.0]; $P = .028$). No other significant differences were found in cardiac function or size 1-year postpartum compared with preconception values.

Conclusions Cardiovascular events are relatively rare 1 year after pregnancy in women with CHD. Women with cardiovascular events during pregnancy are prone to develop cardiovascular events 1-year postpartum and have increased subpulmonary ventricular diameter compared with preconception values. (Am Heart J 2015;169:298-304.)

Women with congenital heart disease (CHD) are prone to develop cardiovascular complications during pregnancy.[1-4] Until now, research has mainly focused on risk prediction of cardiovascular complications during pregnancy, and several prediction models have been developed.[1-4] However, limited data exist regarding the effects of pregnancy on maternal cardiac function and prognosis after pregnancy. Data from a small number of (mostly retrospective) studies have suggested that pregnancy may have an adverse effect on maternal cardiac outcome (with each subsequent pregnancy causing progression of cardiac dysfunction) and that women with adverse cardiac events during pregnancy are at increased risk for cardiac events >6 months after pregnancy.[5-12] Prospective research data are very limited and concern only small study populations.

Therefore, a large prospective multicenter study was conducted to observe the incidence of cardiovascular complications in the first year postpartum and to compare cardiac function parameters prepregnancy and 1-year postpartum in women with CHD.

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Methods

Patient selection

The ZAHARA II study is a prospective multicenter cohort study, conducted between March 2008 and August 2011. All consecutive pregnant women with structural CHD, aged ≥18 years, and presenting in 1 of the 8 participating centers were eligible for enrollment. The methods and primary results have been described elsewhere.[13,14] Women again pregnant before the postpartum follow-up visit were excluded from determination of cardiac outcome, and only the first pregnancy during the study period was included in this article.

Baseline characteristics, pregnancy data, and 1-year postpartum follow-up

Prepregnancy baseline characteristics were collected from medical records during the first antepartum visit. Baseline data included maternal age, underlying congenital anomaly, prior interventions, previous cardiovascular events, medication use, New York Heart Association (NYHA) functional class, echocardiographic recordings, cardiopulmonary aerobic capacity test results (<2 years before conception), 12-lead electrocardiogram, laboratory results, comorbid conditions, and obstetric history. Patients visited the outpatient clinic at 20 and 32 weeks of gestation and 1-year postpartum for clinical evaluation (including NYHA class assessment), standardized echocardiograms (according to study protocol), 12-lead electrocardiogram, and NT-proBNP measurement. In addition, when possible, cardiopulmonary aerobic capacity testing was performed 1-year postpartum.

All echocardiographic recordings were evaluated offline by 4 experienced cardiologists, blinded to the end points. Chamber quantification, valvular function, and systolic and diastolic ventricular function assessment were performed according to the current recommendations as previously described.[13]

Cardiac function and cardiovascular events 1-year postpartum

Cardiovascular events (>6 months after delivery) were assessed during the follow-up visit 1-year postpartum. Primary cardiovascular events as previously defined include any of the following: need for an urgent invasive cardiovascular procedure, heart failure (according to the guidelines of the European Society of Cardiology and documented by the attending physician)[15], new onset or symptomatic tachyarrhythmia or bradyarrhythmia requiring new or extended treatment, thromboembolic events, myocardial infarction, cardiac arrest, cardiac death, endocarditis, and aortic dissection.[13] Echocardiographic changes were defined as deterioration in size or function of subpulmonary or subaortic ventricle, new onset or aggravation of valve regurgitation, or stenosis ≥1 grade (mild to moderate or severe or moderate to severe).

Statistical analysis

For continuous data, means and SD or medians with interquartile range were calculated, depending on their distribution. Absolute numbers and percentages were presented for categorical data. The Student *t* test, Mann-Whitney *U* test, χ^2, or Fisher exact test was used for intergroup comparison as appropriate. For comparison of cardiac function parameters before and after pregnancy, paired Student *t* test or Wilcoxon signed rank test for related samples was used, depending on their distribution. For categorical data, McNemar test for related samples was used. Differences in the rates of late cardiac events were determined using log-rank tests. The current study concerns an analysis of the secondary outcomes of the ZAHARA II study, for which a formal power analysis was not performed. Statistical analysis was performed using STATA software package (version 11; College Station, TX). A 2-tailed *P* value <.05 was considered significant.

The research ethics committee of all participating centers approved the study protocol, and all participating women gave written informed consent. This work is supported by a grant from the Netherlands Heart Foundation (2007B75).The authors are solely responsible for the design and conduct of this study, all study analyses and drafting and editing of the paper.

Results

During the study period, 213 pregnancies (209 singleton and 4 twin pregnancies) in 202 women were observed. Twenty-three women had a second pregnancy during the study period (12 before the postpartum follow-up visit), and 18 women did not return for follow-up. None of the women lost to follow-up died; these patients were all in modified World Health Organization (WHO) risk class 1 or 2, except 1 (modified WHO class 3).

The final study included 172 pregnancies in 172 women. Maternal baseline characteristics and underlying CHD are shown in Table I. Mean age at conception was 28.9 years. Most patients were in NYHA functional class I or II and had a mildly or moderately increased risk of cardiovascular complications during pregnancy as indicated by the modified WHO risk class.[16] Most did not use cardiac medication before pregnancy, and the 2 patients who were on angiotensin-converting enzyme inhibitors discontinued the use because of its teratogenic effects. Systemic ventricular dysfunction (ejection fraction <45%) was present in 6.5% of the women, and subpulmonary ventricular dysfunction (tricuspid annular plane systolic excursion [TAPSE] <16 mm) was seen in 13.8%.

Cardiovascular events 1-year postpartum

Cardiovascular events were seen after 11 pregnancies (6.4 %). The median follow-up time was 1.07 years (interquartile range 0.98-1.32 years).