



Cardiac outcomes after pregnancy in women with congenital heart disease

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Received 17 May 2010
Revised 13 July 2010
Accepted 19 July 2010

ABSTRACT

Objective Women with congenital heart disease (CHD) are at risk for adverse cardiac events during pregnancy; however, the risk of events late after pregnancy (late cardiac events; LCE) has not been well studied. A study was undertaken to examine the frequency and determinants of LCE in a large cohort of women with CHD.

Design Baseline characteristics and pregnancy were prospectively recorded. LCE (>6 months after delivery) were determined by chart review. Survival analysis was used to determine the risk factors for LCE.

Setting A tertiary care referral hospital.

Patients The outcomes of 405 pregnancies were studied (318 women; median follow-up 2.6 years).

Main outcome measures LCE included cardiac death/arrest, pulmonary oedema, arrhythmia or stroke.

Results LCE occurred after 12% (50/405) of pregnancies. The 5-year rate of LCE was higher in women with adverse cardiac events during pregnancy than in those without ($27 \pm 9\%$ vs $15 \pm 3\%$, HR 2.2, $p=0.02$). Women at highest risk for LCE were those with functional limitations/cyanosis (HR 3.9, 95% CI 1.2 to 13.0), subaortic ventricular dysfunction (HR 3.0, 95% CI 1.4 to 6.6), subpulmonary ventricular dysfunction and/or significant pulmonary regurgitation (HR 3.2, 95% CI 1.6 to 6.6), left heart obstruction (HR 2.6, 95% CI 1.2 to 5.2) and cardiac events before or during pregnancy (HR 2.6, 95% CI 1.3 to 4.9). In women with 0, 1 or >1 risk predictors the 5-year rate of LCE was $7 \pm 2\%$, $23 \pm 5\%$ and $44 \pm 10\%$, respectively ($p<0.001$).

Conclusions In women with CHD, pre-pregnancy maternal characteristics can help to identify women at increased risk for LCE. Adverse cardiac events during pregnancy are important and are associated with an increased risk of LCE.

The number of women with congenital heart disease (CHD) continues to increase so that, in the current era, most women with CHD are of or will reach reproductive age.¹ Pregnancy is associated with reversible pregnancy-related increase in blood volume, heart rate and cardiac output^{2–3} and, in some instances, these changes can trigger maternal cardiac deterioration during pregnancy.^{4–7} Outcomes after pregnancy in women with CHD are of particular interest because such women have been exposed to this prolonged haemodynamic stress. In certain medical conditions, pregnancy is felt to act as a physiological stress test and complications during pregnancy identify women at high risk for late events.⁸ Preliminary data from

small retrospective cardiac lesion-specific studies have suggested that pregnancy may have an adverse effect on subsequent maternal cardiac outcomes, perhaps as a result of the haemodynamic burden on ventricular structure and function during pregnancy.^{9–12} A study was therefore undertaken to examine the frequency and determinants of adverse maternal cardiac events late after pregnancy in a large cohort of women with CHD exhibiting a broad spectrum of cardiac disease.

METHODS

Study population

Consecutive pregnant women with CHD receiving care or referred for consultation at our centre between 1995 and 2007 were included, with prospective collection of baseline data and outcomes during pregnancy (antepartum, peripartum and postpartum up to 6 months after delivery). In this prospectively-defined cohort, cardiac outcomes late after pregnancy (>6 months after delivery) were determined retrospectively by chart review and/or contacting referring cardiologists. The following groups were excluded from determination of late outcomes: (1) women in whom pregnancies ended before 20 weeks gestation by miscarriage, termination or fetal death; (2) women who died during pregnancy; and (3) women again pregnant within 6 months of delivery.

Baseline data collection and outcomes during pregnancy

Baseline cardiac data were collected at the first antepartum visit as previously described^{4–5} and included maternal age, nature of cardiac lesions and prior interventions, parity, comorbid conditions (eg, hypertension, diabetes mellitus), history of prior cardiac events (arrhythmia, congestive heart failure, stroke/transient ischaemic attack), presence of cyanosis (oxygen saturation <90%), New York Heart Association (NYHA) functional class, medications and smoking history. Results from 12-lead ECG and transthoracic echocardiogram performed during the first antenatal visit were recorded. A comprehensive transthoracic echocardiogram was performed and was interpreted by an experienced echocardiographer. Subaortic ventricular systolic dysfunction was defined as an ejection fraction <40%.^{5–13} Subpulmonic ventricular systolic function was assessed visually and abnormal subpulmonic ventricular dysfunction was defined as

moderate or greater hypokinesis. Valvular regurgitation and obstruction were assessed by validated methods.^{14 15} Significant valvular regurgitation was defined as moderate or more in severity. Specifically, significant pulmonary regurgitation was defined as laminar retrograde diastolic flow in the pulmonary artery and/or a pressure half time of <100 ms. Left heart obstruction in native and prosthetic valves was defined as mitral valve area <2 cm², aortic valve area <1.5 cm² or peak left ventricular outflow tract gradient >30 mm Hg, consistent with previous reports from our group.⁵

A previously reported maternal cardiac risk index (CARPREG risk score) was used to predict cardiac complications during pregnancy. The score was calculated by assigning one point to each of the following variables: cardiac events prior to pregnancy (arrhythmia, congestive heart failure or stroke/transient ischaemic attack), baseline NYHA functional class >II or cyanosis, systemic ventricular dysfunction and left heart obstruction. Higher scores are associated with worse outcomes.⁵

Maternal pregnancy-related adverse cardiac events (pregnancy cardiac events; PCE) as previously defined were recorded prospectively and included cardiac death, cardiac arrest, pulmonary oedema, sustained symptomatic tachyarrhythmia/bradyarrhythmia requiring treatment and stroke/transient ischaemic attack.⁵ Pregnancy-related non-cardiac adverse outcomes were also prospectively recorded using predefined criteria. Adverse obstetric events included pre-eclampsia or postpartum haemorrhage and adverse fetal and/or neonatal events included premature birth, small-for-gestational-age birth weight, respiratory distress syndrome, intraventricular haemorrhage and fetal or neonatal death.⁵ Maternal placenta-related complications were defined as pre-eclampsia, preterm birth and/or small-for-gestational-age birth.

Maternal cardiac outcomes after pregnancy

Adverse maternal cardiac events late after pregnancy (late cardiac events; LCE) were ascertained by health record review and through direct contact with referring physicians. Follow-up was recorded to the first LCE after the index pregnancy or until the last available clinical follow-up. LCE were defined as any of the following: cardiac death, cardiac arrest, pulmonary oedema (documented on the chest x-ray or by crackles heard over at least one-third of the posterior lung fields), sustained symptomatic tachyarrhythmia/bradyarrhythmia requiring treatment or stroke/transient ischaemic attack.

The frequency of cardiac intervention late after pregnancy was recorded and included cardiac surgery, percutaneous cardiac intervention, catheter ablation for arrhythmia management or pacemaker/internal cardioverter defibrillator implantation. Cardiac interventions were not used as an end point in the multivariate model.

Data analysis

Data analysis was performed using SPSS for Windows Version 16 (SPSS Inc, Chicago, Illinois, USA). Means and standard deviations (SD) or median and interquartile range (IQR) were calculated as appropriate. Categorical data were expressed as absolute counts and percentages. Survival analysis was used to determine predictors of LCE. Differences in the rates of LCE between groups were determined using log rank tests. Univariate predictors of LCE with a *p* value <0.15 were entered into a multivariate Cox proportional hazards model. Subpulmonary ventricular dysfunction and/or significant pulmonary regurgitation were combined into one risk predictor as previously reported.⁶ Collinearity between variables was examined and,

when possible, a suitable variable was created (ie, adverse cardiac events before pregnancy was combined with pregnancy-related adverse events). The proportional hazard assumptions were confirmed for each of the variables entered into the multivariate model. The Cox model was confirmed using a bootstrap analysis. To account for women with more than one pregnancy, the multivariate analysis was repeated with the inclusion of a variable created to identify women with multiple pregnancies to confirm that the results did not substantially change. A *p* value <0.05 was considered statistically significant.

Based on the results of the multivariate model, each statistically significant variable in the model was given a score of one point and the risk points were summated to create a new risk score to estimate the risk of LCE.

RESULTS

During the study period 522 pregnancies in women with CHD were followed at our centre. Of these, 38 pregnancies ended before 20 weeks gestation, there were 4 cardiac deaths during pregnancy, 16 women became pregnant again within 6 months of the index pregnancy and 59 women did not return for follow-up. The women who did not return for follow-up were similar in age to the study population (mean age 28±6 years) but were more likely to have uncomplicated congenital cardiac defects including intracardiac shunts, bicuspid aortic disease or pulmonary stenosis (72% vs 40%).

The final study included 405 pregnancies (318 women, mean maternal age 28±5 years, 66% nulliparous). Pregnancy outcomes in 185 of the 405 pregnancies have been previously reported as part of a national study.⁴ Table 1 summarises the maternal characteristics of the women included in this study and the differences in baseline characteristics and pregnancy-related events between women with or without LCE. Table 2 lists the cardiac diagnosis for the entire cohort. Certain high-risk populations were under-represented in the study including women with dilated aortic roots >40 mm (n=12), women with mechanical heart valves (n=6) and women with severe pulmonary hypertension/Eisenmenger (n=4). Few women reported being in NYHA functional class >II or had resting cyanosis (n=10). Subaortic ventricular dysfunction (n=37, 9%) was most common in women with transposition of the great arteries with atrial switch surgery (n=22), congenitally corrected transposition of the great arteries (n=5) and univentricular hearts (n=4). Left heart obstruction (n=51, 13%) was primarily due to congenital/bicuspid aortic valve stenosis (n=35). The majority of women with subpulmonic ventricular systolic dysfunction and/or pulmonary regurgitation (n=53, 13%) had tetralogy of Fallot (n=37).

PCE occurred in 46 (11%) pregnancies (1 cardiac arrest, 33 arrhythmias, 19 pulmonary oedema and 1 stroke (events not mutually exclusive)). Twenty-one of 48 women (44%) with adverse events before pregnancy had a PCE. Of the 357 women with no adverse events before pregnancy, 25 developed PCE (16% of whom had a LCE). An increased CARPREG risk score, originally created to identify the risk of PCE, was also useful in identifying women with LCE (table 1).

Adverse cardiac events after pregnancy

The median follow-up time was 2.6 years (IQR 1.4–5.2) after pregnancy. LCE developed after 50/405 pregnancies (12%). Table 2 shows the LCE according to the underlying cardiac lesions. Three women (0.007%) died after pregnancy, two of whom had had a PCE. One woman had repaired tetralogy of Fallot with

Table 1 Baseline characteristics

Total number of pregnancies	Cardiac events late after pregnancy		p Value
	N (%) of pregnancies		
	Present (N = 50)	Absent (N = 355)	
Maternal baseline characteristics			
Maternal age (years)	29±6	28±5	0.71
Parity ≥1	31 (62)	148 (42)	0.009
Smoking	4 (8)	25 (7)	0.77
Hypertension or diabetes	1 (2)	5 (2)	0.55
Adverse cardiac events before pregnancy*	14 (28)	34 (10)	0.001
Cardiovascular medications	12 (24)	51 (14)	0.10
NYHA functional class >II or resting cyanosis	3 (6)	7 (2)	0.11
Baseline echocardiographic characteristics			
Subaortic ventricular dysfunction	11 (22)	26 (7)	0.002
Left heart obstruction	10 (20)	41 (12)	0.11
Subpulmonary ventricular dysfunction and/or pulmonary regurgitation	12 (24)	41 (12)	0.02
Mitral and/or aortic regurgitation (≥ moderate in severity)	2 (4)	9 (3)	0.64
Pulmonary artery systolic pressure >40 mm Hg	8 (16)	41 (12)	0.47
Range	7–71	16–51	
CARPREG risk score ⁵			
Risk score ≥1	29 (58)	95 (27)	<0.001
Pregnancy outcomes			
Adverse maternal cardiac event during pregnancy	10 (20)	36 (10)	0.04

*Adverse cardiac events before or after pregnancy were defined as any of the following: cardiac death, cardiac arrest, pulmonary oedema, sustained symptomatic tachyarrhythmia and/or bradyarrhythmia requiring treatment, or stroke or transient ischaemic attack. CARPREG, maternal cardiac risk index; NYHA, New York Heart Association.

severe pulmonary regurgitation and right ventricular systolic dysfunction. She died of sudden cardiac death 2 years after an uneventful pregnancy. The second woman had congenitally corrected transposition of the great arteries and pulmonary atresia. She had a left ventricle to pulmonary artery homograft but had residual subaortic ventricular dysfunction and systemic atrioventricular valve regurgitation. She died 9 years after pregnancy with end-stage heart failure awaiting cardiac transplantation. Her pregnancy was complicated by arrhythmia and pulmonary oedema. The third woman had an unrepaired atrial septal defect, severe left ventricular dysfunction and Wolf-Parkinson-White syndrome and died 4 years after pregnancy, presumably secondary to sudden cardiac death. Her pregnancy was complicated by pulmonary oedema.

The most common LCEs were arrhythmias which occurred in 35 women (14 supraventricular tachycardia, 17 atrial flutter or fibrillation and 4 ventricular tachycardia). Congestive heart failure occurred in 15 women. Overall, the 5-year rate of LCEs was 16±3%. The 5-year rates were higher in women with CARPREG risk scores ≥1 (n=124) than in women with risk scores of 0 (n=280) (30±6% vs 10±2%, *p*<0.001).

Sixty-two pregnancies (15%) were followed by therapeutic cardiac interventions (median time to therapeutic intervention 2.4 years, IQR 1.3–3.8). Ten women had their therapeutic procedure relatively early after delivery (7–12 months); however, only two of these women had PCE. The most common indications for intervention were arrhythmia and/or congestive heart failure (40%) or deterioration in functional capacity (38%). Interventions according to cardiac diagnosis are shown in table 2.

Maternal placenta-related problems occurred in 66 pregnancies (17%) and were similar in women who had LCE and those who did not (25% vs 16%, *p*=0.10).

Risk factors for adverse cardiac events after pregnancy

The univariate predictors of LCE are shown in table 3. Subaortic ventricular dysfunction was more common in women who had LCE (*p*=0.007). While subpulmonary ventricular dysfunction

and/or significant pulmonary regurgitation was not associated with events during pregnancy, it was associated with LCE (*p*=0.002). The CARPREG risk score, originally created to classify PCE, was also useful to assess the LCE with an increased risk of LCE in women with risk score >1 (HR 3.6, 95% CI 2.0 to 6.2, *p*<0.001). The 5-year rates of LCE were significantly higher in women who had PCE than in those who did not (27±9% vs 15±3%, *p*=0.02, figure 1). Compared with women without PCE, women with PCE had more than a twofold risk of LCE (HR 2.2, 95% CI 1.1 to 4.4).

Because of the relationship between adverse cardiac events before pregnancy and PCE, a single variable was created and entered into the multivariate model. In the multivariate model, women at highest risk for LCE were those with NYHA class >II and/or cyanosis (HR 3.9, *p*=0.03), subaortic ventricular dysfunction (HR=3.0, *p*=0.007), subpulmonary ventricular dysfunction and/or pulmonary regurgitation (HR=3.2, *p*=0.002), left heart obstruction (HR=2.6, *p*=0.01) and adverse cardiac events before pregnancy and/or PCE (HR=2.5, *p*=0.006). The survival analysis was repeated with the inclusion of a variable created to identify women with more than one pregnancy recorded in the database. This variable was not significant in the final model and the predictors of LCE remained unchanged.

A novel risk score was created based on the above risk factors, and each predictor as described above in the multivariate model was assigned one point. In women with 0, 1 or >1 risk factors the 5-year rate of LCEs was 7±2%, 23±5% and 44±10%, respectively (*p*<0.001, figure 2).

DISCUSSION

Although late outcomes have been studied in various congenital cardiac lesions individually, no previous large studies have specifically addressed LCE after pregnancy in women of child-bearing age with CHD. This group of women is important because they have been exposed to a prolonged but reversible cardiovascular stress. In this large study, most women with CHD did well after pregnancy and mortality was rare. However,

Table 2 Maternal adverse cardiac events after pregnancy according to cardiac diagnosis

Total	Number of pregnancies				
	Total pregnancies (N) 405	Cardiac events late after pregnancy*		Cardiac interventions*	
		50	Types of cardiac events	62	Types of cardiac events
Shunt lesions					
Repaired	41	3	2 Arr, 1 HF	2	1 EP, 1 Surg
Unrepaired	46	5	3 Arr, 1 Arr+CD, 1 S	13	1 EP, 11 Cath, 1 Surg
Tetralogy of Fallot/DORV repaired	70	9	4 Arr, 3 HF, 1 Arr+CA, 1 CD	12	12 Surg
Aortic coarctation					
Repaired	50	4	2 Arr, 2 HF	2	2 Surg
Unrepaired	2	0	—	1	1 Cath
Congenital aortic stenosis					
Repaired	20	1	1 Arr	4	4 Surg CD, 1 S
Unrepaired	25	4	1 Arr, 3 HF	11	11 Surg
Transposition of great arteries	33	7	6 Arr, 1 HF	5	1 EP, 2 Cath, 2 PM/ICD
Pulmonary stenosis					
Repaired	8	0	—	0	—
Unrepaired	15	0	—	0	—
Marfan syndrome	16	0	—	2	2 Surg
Ebstein anomaly					
Repaired	2	0	—	0	—
Unrepaired	13	4	4 Arr	2	1 EP, 1 Surg
Atrioventricular septal defect repaired	13	1	1 Arr	2	2 Surg
Other diagnosis†					
Repaired	6	0	—	0	—
Unrepaired	10	1	1 HF	0	—
Hypertrophic cardiomyopathy	14	4	1 Arr, 2 HF, 1 Arr+HF	5	1 Cath, 2 PM/ICD, 1 Surg, 1 HTX
Univentricular heart	11	4	4 Arr	0	—
Congenitally corrected transposition	6	1	1 Arr+HF+CD	0	—
Cyanotic patients	4	2	2 Arr	1	1 Surg

Adverse cardiac events are not mutually exclusive.

*Adverse events late after pregnancy: cardiac events (Arr, HF, CD, CA, S) and interventions (Surg, Cath, PM/ICD, EP).

†Other diagnosis: congenital mitral valve disease (n=1); anomalous pulmonary vein drainage (n=3); dextrocardia (n=3); sinus of Valsalva aneurysm (n=2); congenital coronary anomaly (n=4); congenital absence of pericardium (n=1); idiopathic cardiomyopathy and severe pulmonary regurgitation (n=2).

Arr, arrhythmia; CA, cardiac arrest; Cath, interventional procedure; CD, cardiac death; DORV, double outlet right ventricle; EP, electrophysiology study with ablation; HF, congestive heart failure; HTX, heart transplant; PM/ICD, device implantation; S, stroke/transient ischaemic attack; Surg, cardiovascular surgery.

approximately 1/10 pregnancies were followed by a LCE, of which arrhythmias and heart failure were the most common events. Women with poor baseline functional ability and/or

cyanosis, ventricular dysfunction and left ventricular outflow tract obstruction were at highest risk for LCE. There were common risk factors that predict both the risk of adverse events

Table 3 Predictors of adverse maternal cardiac events after pregnancy

	Univariate analysis		Multivariate analysis*	
	HR (95% CI)	p Value	HR (95% CI)	p Value
Maternal baseline characteristics				
Maternal age (years)	1.0 (0.9 to 1.0)	0.56		
Parity ≥ 1	1.7 (0.9 to 3.0)	0.08		
Smoking	0.9 (0.3 to 2.5)	0.86		
Hypertension or diabetes	1.4 (0.2 to 10.2)	0.74		
Adverse cardiac events before pregnancy	3.5 (1.9 to 6.4)	<0.001		
Cyanosis	2.4 (0.6 to 9.8)	0.24		
NYHA functional class >II or resting cyanosis	4.3 (2.0 to 0.3)	<0.001	3.9 (1.2 to 13.0)	0.03
Pregnancy-related outcomes				
Pregnancy-related adverse cardiac events	2.2 (1.1 to 4.4)	0.02		
Adverse cardiac events before pregnancy and/or pregnancy-related adverse cardiac events	3.0 (1.7 to 5.4)	<0.001	2.6 (1.3 to 4.9)	0.005
Baseline echocardiographic characteristics				
Subaortic ventricular dysfunction	3.1 (1.6 to 6.1)	0.001	3.0 (1.4 to 6.6)	0.007
Subpulmonary ventricular dysfunction and/or significant pulmonary regurgitation	2.2 (1.1 to 4.2)	0.02	3.2 (1.6 to 6.6)	0.002
Left heart obstruction	1.7 (0.9 to 3.4)	0.13	2.6 (1.2 to 5.2)	0.01
Mitral and/or aortic regurgitation (moderate or greater in severity)	1.4 (0.3 to 5.8)	0.65		
Pulmonary artery systolic pressure >40 mm Hg	1.3 (0.6 to 2.8)	0.32		

*Variables entered into the multivariate model included multiparity, NYHA functional class >II or cyanosis, subaortic ventricular dysfunction, subpulmonary ventricular dysfunction and/or pulmonary regurgitation, left heart obstruction and adverse cardiovascular events before pregnancy or pregnancy-related adverse cardiac events.

A risk score was created based on the significant predictors of adverse maternal cardiac events identified in the multivariate model. Each variable from the multivariate model was assigned one point and points were summated to create a risk score to estimate the risk of late adverse cardiac events (see Figure 2).

NYHA, New York Heart Association.

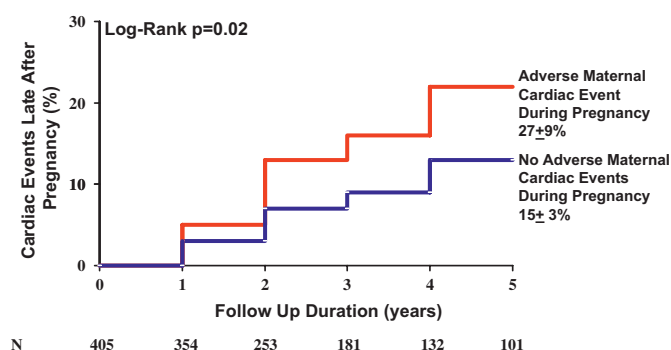


Figure 1 Incidence of adverse cardiac events late after pregnancy according to pregnancy-related adverse cardiac events (time 0 = date of pregnancy). Adverse cardiac events were defined as any of the following: cardiac death, cardiac arrest, pulmonary oedema, sustained symptomatic tachyarrhythmia and/or bradyarrhythmia requiring treatment, or stroke or transient ischaemic attack.

during and after pregnancy. Adverse maternal cardiac events after pregnancy were more common in women who had cardiac events during pregnancy.

Because of the nature of the underlying cardiac lesions and the prior catheter and surgical procedures, adults with CHD have a propensity for arrhythmias and are at risk of developing ventricular dysfunction. In non-pregnant adult patients with CHD, arrhythmias and heart failure are common cardiac complications,^{1–16} similar to the types of adverse cardiac events observed in our population. In a number of congenital cardiac conditions, heart failure and arrhythmias can be inter-related and arrhythmias, including atrial arrhythmias, can be markers of important haemodynamic deterioration.^{17–20} Thus, identifying women at highest risk is important so that surveillance can be tailored to the individual.

Risk factors for LCE were similar to those previously identified as risk predictors of pregnancy-related adverse events including functional status and cyanosis,^{4–5} subaortic or subpulmonary ventricular dysfunction^{5–6} and left heart obstruction.^{5–9–21–22} This finding suggests a link between the inability of the heart to adapt to haemodynamic challenges such as pregnancy and worse

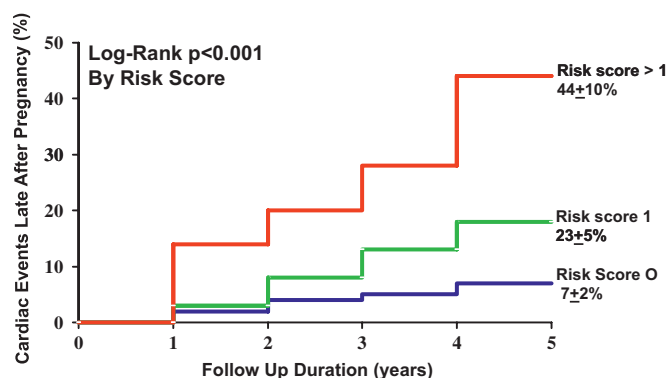


Figure 2 Incidence of adverse cardiac events late after pregnancy according to maternal risk score. The risk score for late events was calculated based on the sum of risk predictors. Each predictor was assigned one point. Predictors included in the risk score were: New York Heart Association functional class >II and/or resting cyanosis, subaortic ventricular dysfunction, subpulmonary ventricular dysfunction and/or significant pulmonary regurgitation, left heart obstruction and cardiac events before or during pregnancy. Adverse cardiac events were defined as any of the following: cardiac death, cardiac arrest, pulmonary oedema, sustained symptomatic tachyarrhythmia and/or bradyarrhythmia requiring treatment, or stroke or transient ischaemic attack.

late outcomes. An important finding in our study demonstrated that, although the identifiable cardiovascular changes of pregnancy resolve after delivery, adverse cardiac events that occur during this haemodynamic stress appear to have importance, increasing the risk of LCE.

There are a number of mechanisms which may explain this association between baseline maternal cardiac variables, PCE and LCE. The haemodynamic load of pregnancy may serve as a physiological stress test⁸ and, in women with underlying heart disease, may unmask limited cardiac reserve. Conceptually, this may be similar to the observation that women with placental syndromes during pregnancy are at increased risk of atherosclerotic disease late in life. In these women, pregnancy unmasks an underlying ‘abnormal metabolic milieu’ that also predisposes them to pregnancy complications and to atherosclerotic disease much later after pregnancy.^{23–24} Alternatively, the prolonged haemodynamic stress of pregnancy may directly impact cardiac function. In the normal heart there is an increase in ventricular wall stress and an associated deterioration in cardiac function during pregnancy.²⁵ In a similar fashion, increases in wall stress may impact the structurally abnormal heart and this may result in similar or even worse deterioration in cardiac function. Supporting this concept is the finding, reported by others, that systemic ventricular function can irreversibly deteriorate after pregnancy in women with transposition of the great arteries and Mustard operations.¹¹ In our series, women with either subaortic or subpulmonic ventricular dysfunction were at highest risk for LCE. The prolonged volume load on the heart may also affect the myocardium in a fashion analogous to the effect of valvular regurgitation, which is recognised to lead over time to ventricular dilation and dysfunction. In women with tetralogy of Fallot it has been suggested that pregnancy can affect right ventricular volumes.¹⁰ Volume overload and myocyte stretch have been shown to be a stimulus for pathophysiological myocardial processes such as apoptosis, fibrosis and arrhythmogenesis.^{26–27} Finally, adverse cardiac events themselves may directly affect the myocardium. Heart failure is associated with increases in norepinephrine and epinephrine which have been shown to have direct cardiotoxic effects including myocyte injury.²⁸ Clinically, it has been shown that cardiac outcomes are worse in patients with recurrent admissions for heart failure.²⁹ Continuing to clarify how pregnancy affects the diseased heart is important for risk stratification and to identify potential therapeutic targets.

Our findings raise a number of important clinical considerations. Before pregnancy, women at high risk for LCE should be counselled not only about the risks of adverse cardiac events during pregnancy but also regarding the potential for adverse cardiac events after pregnancy. The current risk score should be used in conjunction with known lesion-specific data on outcomes. For instance, women with Marfan syndrome and dilated aortic roots were under-represented in this study but are known to be at high risk for complications. In these cases, lesion-specific outcomes need to be incorporated into counselling. Once women become pregnant, those at high risk should receive closer surveillance not only during pregnancy but also late after delivery. Because adverse events during pregnancy are associated with higher rates of late events, it is important to re-evaluate the maternal cardiac status of women with PCE more closely after pregnancy.

Limitations

A selection bias probably exists as a small number of the women initially enrolled in our prospective study of pregnancy outcomes

were not included in this long-term follow-up study because they did not receive long-term follow-up at our centre. Women not followed at our centre were more likely to have less complicated forms of heart disease. This pattern of follow-up reflects the nature of our clinic and the American College of Cardiology/American Heart Association guidelines for the follow-up in patients with simple CHD.³⁰ Because of this, our estimate of the prevalence of late complications would overestimate rates in cohorts of women with simple CHD only. However, predictors of late outcomes are not likely to be affected by this selection bias.

Importantly, women with some high-risk lesions such as Eisenmenger syndrome, Marfan syndrome with dilated aortic roots or mechanical heart valves were under-represented in this study. Not only are these lesions less common in general, but women with high-risk lesions are often advised to avoid pregnancy. The impact of adverse cardiac events during pregnancy on late outcomes in this high-risk group cannot be determined.

This study did not examine all adverse events associated with pregnancy or with late outcomes. During and after pregnancy, some women suffer significant functional deterioration without frank pulmonary oedema or have prolonged hospital admissions. Thus, there are other morbidities beyond those defined in our study, and these may be meaningful for the individual patient.

Late outcome data were collected retrospectively and therefore this study is also subject to the inherent limitations of a retrospective study. Baseline data had been collected prospectively between 1994 and 2007 and therefore newer echocardiographic measures of right ventricular function such as tissue Doppler were not available.

Although women with adverse events before and during pregnancy were at higher risk of LCE, this study did not include a matched control cohort and therefore was not designed to determine the impact of pregnancy on the natural history of the cardiac conditions studied.

CONCLUSION

Women with CHD are at risk of cardiac complications after pregnancy. The risk of such events can be predicted by identification of maternal factors that predict both the risk of adverse events during and after pregnancy. Adverse cardiac events during pregnancy are important and women who develop adverse cardiac events during pregnancy are at increased risk of LCE.

Funding This work is supported by operating grants from Heart and Stroke Foundation of Canada (NA 5927, NA 5662) and Canadian Institutes of Health Research (53030, 93722). SCSis supported by the Ramsay Gunton Professorship in Cardiology of the Schulich School of Medicine and Dentistry, University of Western Ontario. The University of Toronto Pregnancy and Heart Disease Research Program acknowledges a generous donation from Mrs Josephine Rogers.

Competing interests None.

Ethics approval This study was conducted with the approval of the University Health Network and Mount Sinai Hospital, Toronto, Canada and all subjects gave informed consent.

Contributors All authors met authorship criteria and gave their final approval of the manuscript.

Provenance and peer review Not commissioned; externally peer reviewed.

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