Title

Cardiovascular events more than 6 months after pregnancy in patients with congenital heart disease.

Journal

Open Heart, 10(2)

ISSN

2053-3624

Authors

Schultz, Hayley
Sobhani, Nasim
Blissett, Sarah
et al.

Publication Date

2023-09-01

DOI

10.1136/openhrt-2023-002430

openheart

Cardiovascular events more than 6 months after pregnancy in patients with congenital heart disease

Hayley Schultz ,[1,2] Nasim C Sobhani,[3] Sarah Blissett,[3,4] Vidhushei Yogeswaran ,[5] Jessica Hong,[3] Ian S Harris,[3] Nisha Parikh,[6] Juan Gonzalez,[3] Anushree Agarwal[7]

To cite: Schultz H, Sobhani NC, Blissett S, *et al*. Cardiovascular events more than 6 months after pregnancy in patients with congenital heart disease. *Open Heart* 2023;**10**:e002430. doi:10.1136/openhrt-2023-002430

Received 22 July 2023
Accepted 8 August 2023

[1]School of Medicine, University of California, San Francisco, California, USA
[2]Obstetrics, Gynecology, and Reproductive Sciences, University of California, San Diego, La Jolla, California, USA
[3]Obstetrics, Gynecology, and Reproductive Sciences, University of California, San Francisco, California, USA
[4]Department of Medicine, Division of Cardiology, Western University, London, Ontario, Canada
[5]Division of Cardiology, University of Washington Medical Center, Seattle, Washington, USA
[6]Department of Medicine, Division of Cardiology, University of California, San Francisco, California, USA
[7]Cardiology, University of California, San Francisco, California, USA

Correspondence to
Dr Anushree Agarwal; anu.agarwal2@ucsf.edu

ABSTRACT

Objectives Patients with congenital heart disease (CHD) are increasingly pursuing pregnancy, highlighting the need for data on late cardiovascular events (more than 6 months after delivery). We aimed to determine the incidence of late cardiovascular events in postpartum patients with CHD and evaluate the accuracy of the existing risk scores in predicting these events.

Study design We identified patients with CHD who delivered between 2008 and 2020 at a tertiary centre and had follow-up data for greater than 6 months post partum. Late cardiovascular events were defined as heart failure, arrhythmia, thromboembolic events, endocarditis, urgent cardiovascular interventions or death. Survival analysis and Cox proportional model were used to estimate the incidence of late cardiovascular events and determine the hazard ratio of factors associated with these events.

Results Of 117 patients, 19% had 36 late cardiovascular events over a median follow-up of 3.8 years. Annual incidence of any late cardiovascular event was 5.7%. Hazards of late cardiovascular events were significantly higher among those with higher Cardiac Disease in Pregnancy Study (CARPREG) II and Zwangerschap bij Aangeboren HARtAfwijking-Pregnancy in Women With Congenital Heart Disease (ZAHARA) risk scores and among patients with prepregnancy New York Heart Association class≥II. C-statistic to predict the late cardiovascular events was highest for ZAHARA (0.7823), followed by CARPREG II (0.6902) and prepregnancy New York Heart Association class≥ II (0.6677).

Conclusions Currently available risk tools designed for prognostication during the peripartum period can also be used to determine risks of late maternal cardiovascular events among those with CHD. These findings provide important new information for counselling and risk modification.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Several contemporary risk prediction scores were developed to determine risk of peripartum adverse events (in pregnancy and up to 6 months post partum), but their utility in predicting late maternal cardiovascular events has not been evaluated.

WHAT THIS STUDY ADDS

⇒ Twenty-five per cent of previously pregnant patients with congenital heart disease in the study population had a late cardiovascular event by 4.4 years of postpartum follow-up. Prepregnancy New York Heart Association class and the contemporary risk prediction scores Cardiac Disease in Pregnancy Study II and Zwangerschap bij Aangeboren HARtAfwijking-Pregnancy in Women With Congenital Heart Disease were independent predictors of these late cardiovascular events and may be used for prognostication.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These data provide valuable information to guide clinicians on preconception counselling, risk modification and long-term surveillance for late cardiovascular events among those with congenital heart disease.

INTRODUCTION

Due to advances in cardiac care, an increasing number of patients with congenital heart disease (CHD) are now reaching childbearing age.[1 2] The haemodynamic changes of pregnancy include increases in plasma volume, heart rate and cardiac output, which may not be well tolerated by these patients.[3] Those with CHD can experience adverse cardiovascular outcomes during pregnancy, within 6 months post partum,[4 5] and even after 6 months postpartum (late cardiovascular events).[6 7] Although important for appropriate counselling and management, information regarding incidence and predictors of late cardiovascular events is limited.

One prior study demonstrated that prepregnancy maternal characteristics, such as ventricular/valvular function, cyanosis and adverse cardiovascular events during or before pregnancy are independent predictors of late cardiovascular events.[7] However, these data were published prior to the availability of many of the contemporary pregnancy-related risk scores, such as the modified

WHO classification (mWHO), Cardiac Disease in Pregnancy Study (CARPREG) score, CARPREG II score and Zwangerschap bij Aangeboren HARtAfwijking-Pregnancy in Women With Congenital Heart Disease (ZAHARA) score.[8–11] These scores were developed to determine risk of peripartum adverse events (in pregnancy and up to 6 months post partum), but their utility in predicting late maternal cardiovascular events has not been evaluated. Moreover, most research to date on peripartum cardiovascular events has evaluated a broad variety of native and acquired heart disease, risking overgeneralisation of the vast range of physiology. Understanding utility of these risk scores in the CHD population could allow use of familiar and validated tools to facilitate counselling and risk modification for these patients while considering late cardiovascular risks.[4 5]

To this end, we used a database of pregnant patients with CHD managed by a multidisciplinary cardio-obstetric team at a tertiary centre to determine the (1) rates and predictors of late cardiovascular events and (2) accuracy of the contemporary risk scores in predicting these events.

MATERIALS AND METHODS

This study included all patients with CHD followed at the University of California, San Francisco (UCSF) multidisciplinary Pregnancy and Cardiac Treatment (PACT) programme. Founded in 2008, the PACT programme is run by a multidisciplinary group of specialists in maternal–fetal medicine, cardiology, obstetric anesthesiology and nursing managing preconception, antepartum, intrapartum and postpartum patients with CHD and other cardiac disease. Patients with CHD who delivered at UCSF between August 2008 and March 2020 were eligible for study inclusion. Those with isolated patent foramen ovale or isolated mitral valve prolapse were excluded, as previously described.[8 12] For patients who had multiple pregnancies during the study period, only the first pregnancy was included. Pregnancies that did not continue beyond 20 weeks' gestation were excluded. Patients who died during pregnancy or within first 6 months post partum were excluded.

All data were retrospectively collected from the electronic medical record, with review of obstetric and cardiovascular consultation notes, radiographic and echocardiographic reports and scanned records from referring physicians. Study data were collected and managed using the Research Electronic Data Capture tool, a secure, web-based software platform designed to support data capture for research studies.[13]

The primary outcome was a composite outcome of any late cardiovascular events, defined as an adverse cardiovascular event occurring more than 6 months after delivery. Adverse cardiovascular events included: (1) heart failure or pulmonary oedema (defined by diuretic use, chest X-ray documentation of pulmonary oedema or physical examination documentation of rales heard more than one-third up lung fields)[8 9]; (2) sustained arrhythmia requiring treatment, documented by ECG, or regarded as symptomatic and significant by a cardiologist at the time of the event; (3) thromboembolic events, including myocardial infarction or cerebrovascular accident; (4) bacterial endocarditis; (5) the need for urgent invasive cardiac intervention or (6) any cardiovascular death. Any planned cardiac intervention, such as a planned closure of atrial septal defect diagnosed during pregnancy or planned valvular intervention, was excluded.

Predictor variables included maternal demographic characteristics, prepregnancy cardiac characteristics and pregnancy-related events. Demographic variables included age, race/ethnicity, insurance status, body mass index and multiparity. Prepregnancy cardiac characteristics were included based on the most recently available information up to 2 years before the last menstrual period. For patients who had no prepregnancy data available, information available during the first pregnancy-related visit was used to determine prepregnancy characteristics. Prepregnancy cardiac characteristics included type of CHD (severe or non-severe),[14] New York Heart Association (NYHA) functional class, prior cardiovascular events (heart failure, arrhythmia or thromboembolic events), prior cardiovascular interventions, chronic hypertension, diabetes mellitus and use of any cardiac medication. Echocardiographic data collected included systemic ventricular function, systemic ventricular ejection fraction, Doppler quantification of obstructive and regurgitant lesions, and right ventricular systolic pressure estimates. mWHO group, CARPREG, CARPREG II and ZAHARA risk scores were calculated for each patient.[8–11]

Pregnancy-related events included antepartum cardiovascular events, postpartum cardiovascular events and perinatal events. Antepartum events included any cardiovascular event (as defined above) that occurred between the patient's last menstrual period and the day of delivery, and postpartum events included any cardiovascular event that occurred from the day after delivery through 6 months post partum.

Dichotomous variables were presented as number with percentage, and continuous variables as mean±SD or median with IQR as appropriate. Kaplan-Meier survival analysis was performed to estimate the incidence of late cardiovascular events. Patients who had the event were censored at the time of their first event; patients who did not have the event were censored at the time of their last follow-up. Unadjusted and adjusted Cox proportional hazard ratio (HR) with 95% confidence intervals (CI) were calculated to determine predictors of late cardiovascular events. Concordance statistic (C-statistic) with 95% CI was used to evaluate how well the various risk scores and other variables predict late cardiovascular events. Two-tailed $p<0.05$ was considered statistically significant.Statistical testing was performed with the use of Stata software V.14.2.

Table 1 Distribution of maternal congenital heart disease (CHD) of 117 patients by primary lesion

Congenital lesion	No (%)
Non-severe disease	**75 (64.1)**
Atrial septal defect	17
Ventricular septal defect	11
Patent ductus arteriosus	3
Partial anomalous pulmonary venous return	4
Coarctation of the aorta, repaired	7
Aortic valve disease±bicuspid aortic valve	19
Pulmonary stenosis	10
Double chamber right ventricle	2
Tricuspid valve stenosis	1
Subaortic stenosis	1
Severe disease	42 (35.9)
Interrupted aortic arch	1
Pulmonary arterial hypertension with CHD	1
Tetralogy of Fallot	18
Transposition of the great arteries (8 D-loop, repaired; 3 L-loop, unrepaired)	14
Double outlet right ventricle	2
Truncus arteriosis	2
Univentricular physiology	4

RESULTS

A total of 502 consecutive pregnancies complicated by maternal cardiac disease were identified between 2008 and 2020. Of these with native and acquired cardiac disease, 176 pregnancies among 149 patients had a diagnosis of CHD. Finally, 117 out of the 149 patients with CHD had follow-up data for more than 6 months post partum and were included. About one-quarter of these patients did not have prepregnancy data; data available during their first pregnancy evaluation was used. There were 42 (36%) patients with severe CHD. The most common CHD lesions were aortic valve disease (16%), atrial septal defect (15%), tetralogy of Fallot (15%) and transposition of the great arteries (12%) (table 1). Baseline demographics, prepregnancy cardiac characteristics and pregnancy-related events are summarised in table 2.

Rates and predictors of late cardiovascular events

Median follow-up time was 3.8 years (IQR 1.8–6.5). A total of 22 patients (19%) had 36 late cardiovascular events, most commonly arrhythmia (15, 42% of events) and heart failure (11, 31% of events). An urgent cardiac intervention was needed in four patients and included ascending aortic pseudoaneurysm repair, pulmonary valve replacement in the setting of endocarditis, radiofrequency arrhythmia ablation procedure and aortic valve and conduit replacement. Thromboembolic events and infective endocarditis each occurred in three patients, and there were no deaths. Annual incidence of any late cardiovascular event was 5.7%, heart failure was 5.3% and arrhythmia 5.5%. Using Kaplan-Meier survival analysis, we estimated that 25% of patients with CHD will experience a cardiovascular event by 4.4 years post partum.

Among the demographic, prepregnancy and pregnancy-related characteristics, the incidence of late cardiovascular events was higher for those with prepregnancy NYHA class≥II (56.3% vs 12.9%, p<0.001), any prepregnancy cardiovascular event (39.3% vs 12.4%, p=0.004), any cardiovascular event during pregnancy (50.0% vs 14.6%, p=0.005), and any cardiovascular event within 6 months post partum (75.0% vs 16.8%, p=0.021). Annual incidence of late cardiovascular events was significantly higher with higher pregnancy risk scores when

Table 2 Patient characteristics (N=117)

	No of patients
Demographic characteristics	
Maternal age, years	30±6.1
Non-white ethnicity	65 (55.5)
Federally funded insurance*	17 (20.5)
Body mass index (kg/m^2)	30±5.8
Prepregnancy characteristics	
NYHA class≥II	16 (13.7)
Any prepregnancy cardiovascular event†	28 (23.9)
Any prior cardiovascular intervention‡	85 (72.7)
Ejection fraction <55%*	16 (19.3)
Chronic hypertension	10 (8.6)
Pre-existing diabetes mellitus	1 (1.0)
mWHO group>II	63 (53.8)
CARPREG score≥1	33 (28.2)
CARPREG II score 0–2	84 (71.8)
CARPREG II score≥3	31 (28.2)
ZAHARA score 0–0.50	57 (48.7)
ZAHARA score 0.51–1.50	27 (23.1)
ZAHARA score≥1.51	33 (28.2)
Any prepregnancy cardiac medication§	25 (21.4)
Prepregnancy aspirin use	24 (20.5)
Pregnancy-related events	
Any antepartum cardiovascular event†	14 (12.0)
Any postpartum¶ cardiovascular event†	4 (3.4)

Data for continuous variables presented as median±IQR.
Data for dichotomous variables presented as N (%).
*Total N=83 due to missing data.
†Includes prepregnancy congestive heart failure, arrhythmia, thromboembolic or cerebrovascular event.
‡Includes surgical, transcatheter or arrhythmic intervention.
§Includes ACE inhibitor, diuretic, beta blocker, anticoagulant, digoxin.
¶Delivery through 6 months post partum.
CARPREG, Cardiac Disease in Pregnancy Study; mWHO, modified WHO classification ; NYHA, New York Heart Association; ZAHARA, Zwangerschap bij Aangeboren HARtAfwijking.

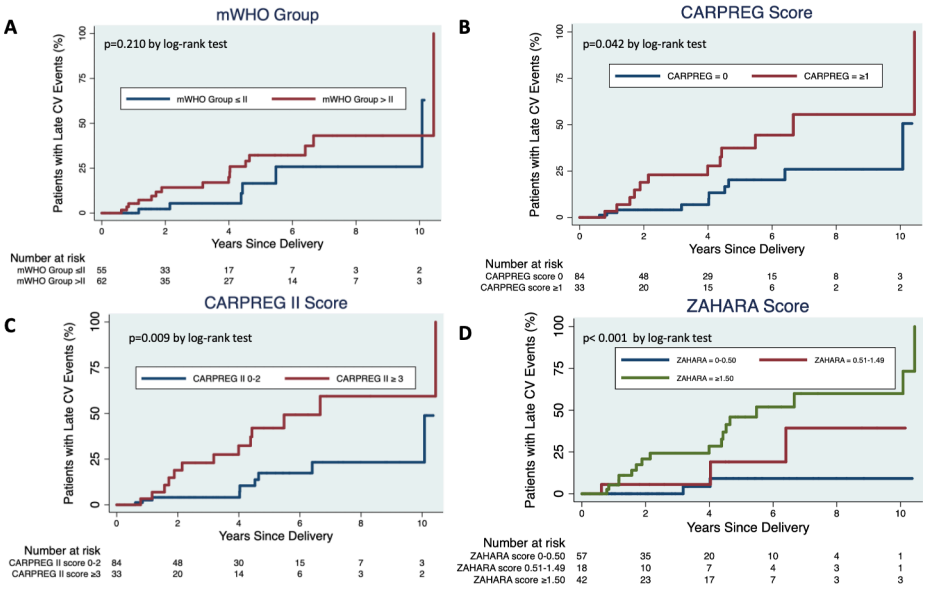

Figure 1 Late cardiovascular (CV) event rates by risk score Kaplan-Meier CV event rate by (A) mWHO class, (B) CARPREG score, (C) CARPREG II score and (D) ZAHARA score. CARPREG, Cardiac Disease in Pregnancy Study; mWHO, modified WHO; ZAHARA, Zwangerschap bij Aangeboren.

using CARPREG (3.5% if score<1 vs 9.8% if score≥1, p=0.044), CARPREG II (3.2% if score<3 vs 10.7% if score≥3, p=0.009) and ZAHARA (1.0% if score<0.51 vs 5.0% if score 0.51–1.49 vs 11.5% if score ≥1.50, p=0.0007). However, incidence of late events was not significantly different between different mWHO groups (3.5% if mWHO≤II vs 6.9% if mWHO>II 1, p=0.225) (figure 1).

Univariate and multivariate HR for the various risk scores and other key characteristics are shown in figure 2. After multivariate adjustment, the HR for late cardiovascular events remained significant for prepregnancy NYHA class ≥II, CARPREG II score ≥3 and ZAHARA score ≥1.50. The C-statistic to predict the late cardiovascular events was highest for ZAHARA score, followed by CARPREG II score and prepregnancy NYHA class (table 3).

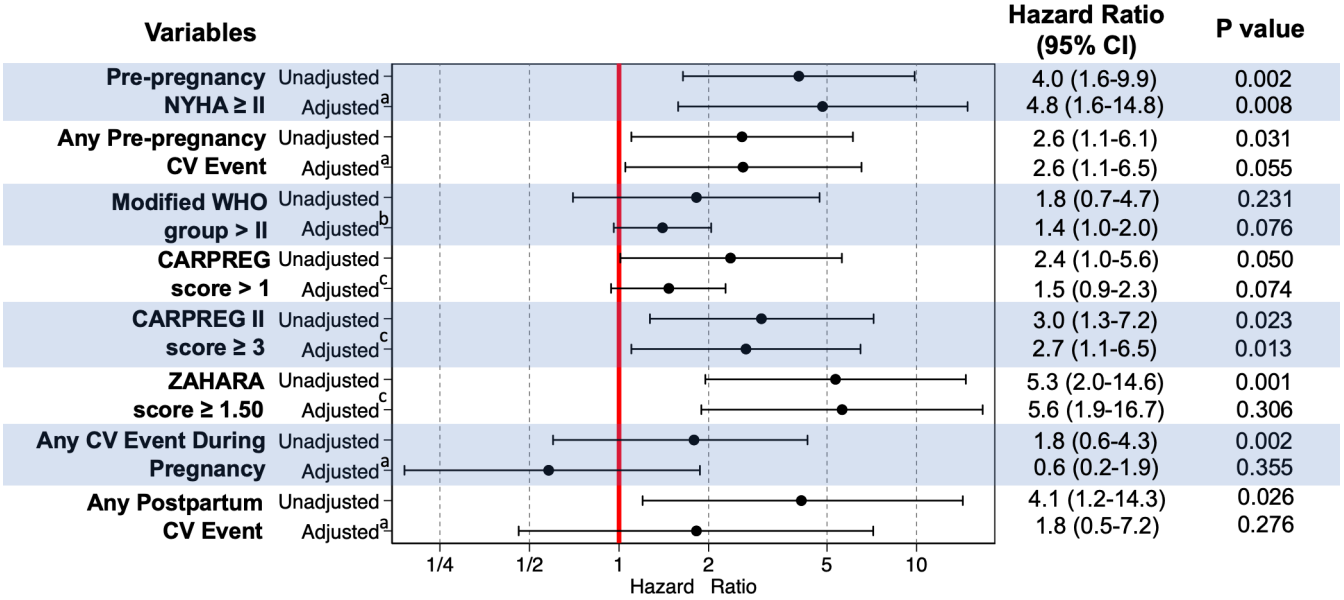

Figure 2 Unadjusted and adjusted HR for late cardiovascular (CV) events (>6 months after delivery) among postpartum patients with congenital heart disease (CHD) aAdjusted for maternal age, prepregnancy NYHA class, prepregnancy CV events, any CV event during pregnancy or any postpartum CV event within 6 months after delivery. bAdjusted for maternal age, prepregnancy NYHA class, any CV event during pregnancy and any postpartum CV event within 6 months after delivery cAdjusted for maternal age, any CV event during pregnancy and any postpartum CV event within 6 months after delivery. CARPREG, Cardiac Disease in Pregnancy Study; NYHA, New York Heart Association; ZAHARA, Zwangerschap bij Aangeboren.

Table 3 C-statistics for predictors of late cardiovascular (CV) events

	C-statistic	95% CI	P value
ZAHARA score	0.7823	0.6947 to 0.8710	Reference
CARPREG II score	0.6902	0.5773 to 0.8031	0.1300
Prepregnancy NYHA class	0.6677	0.5593 to 0.7761	0.0800
Modified WHO group	0.6163	0.5085 to 0.7241	0.0274
Any prepregnancy CV event	0.6605	0.5468 to 0.7743	0.0213
CARPREG score	0.6622	0.5478 to 0.7767	0.0203
Any CV event during pregnancy	0.6222	0.5192 to 0.7253	0.0110
Any CV event <6 months post partum	0.5629	0.4888 to 0.6370	0.0001

CARPREG, Cardiac Disease in Pregnancy Study; NYHA, New York Heart Association; ZAHARA, Zwangerschap bij Aangeboren.

COMMENT

Principal findings

In this single tertiary centre cohort of previously pregnant patients with CHD, we found that approximately one in four have a late cardiovascular event by 4.4 years of postpartum follow-up. When adjusting for key confounding variables, independent predictors of late cardiovascular events were prepregnancy NYHA class≥II, CARPREG II score≥3 and ZAHARA score≥0.51. Of the existing risk scores developed for predicting risk of peripartum adverse events, the ZAHARA and CARPREG II scores had highest C-statistic for predicting late cardiovascular events. These data provide valuable information to guide clinicians on preconception counselling, risk modification and long-term surveillance for late cardiovascular events among those with CHD.

Results in the context of what is known

The overall incidence of late cardiovascular events in our study was 75% higher than that reported in a Canadian cohort (21% vs 12%) despite similar complexity of CHD population (~28% patients in both studies had CARPREG risk score≥1).[7] Differences in baseline patient characteristics (higher prevalence of prepregnancy NYHA class≥II, chronic hypertension, prepregnancy cardiovascular event in our study), institutional referral patterns and management decisions might account for some of the disparity. Despite these differences, both our findings and the prior report noted arrhythmia and heart failure as the most common late cardiovascular events. This is unsurprising, given that these two events are the most frequent peripartum cardiovascular events in the maternal CHD population and in the non-pregnant CHD population.[7–10 12 15–21] Furthermore, arrhythmias and heart failure are known to be inter-related, with one complication typically serving as a marker or a risk factor for the other.

Since the initial description of CARPREG score in 2001,[8] multiple additional scoring systems (ie, ZAHARA,[9] mWHO[11 22] and CARPREG II[10]) have been developed and are being used to predict risk of peripartum cardiovascular events among those with maternal cardiac disease. In this study, we expand on the utility of these scoring systems to provide the data regarding their ability to predict late cardiovascular events that occur more than months post partum. We found that CARPREG II and ZAHARA had the highest C-statistics for prediction and that the mWHO class was not associated with risk of late cardiovascular events. The mWHO class is unique in including only the anatomic details of the cardiac diagnosis. In contrast, the other risk scores include clinical history (eg, prepregnancy cardiac events) and physiological status (eg, prepregnancy NYHA class) in their prediction model. Since scores relying on cardiac history and physiological class (CARPREG II and ZAHARA) more accurately predicted late cardiovascular events than mWHO in our study, we hypothesise that the clinical history and NYHA class is likely more important than the anatomical CHD diagnosis for prognostication of late outcomes after pregnancy.

Clinical implications

Our findings provide important data for the growing population of patients with CHD in their childbearing decades. All patients with CHD of childbearing potential should have routine counselling regarding cardiovascular risks during pregnancy, in the immediate postpartum period, and in the long-term following a pregnancy. A detailed history about the patient's functional status and prior cardiac events should be the foundation of such visits. Additionally, for those contemplating pregnancy or who are newly pregnant, efforts should be made to obtain in-depth cardiac evaluation (eg, comprehensive echocardiogram, ECG or cardiac rhythm monitoring) and a detailed medication history in order to determine the patient's specific pregnancy risk scores. Since the American Heart Association and American College of Cardiology generally recommend multidisciplinary care at a comprehensive CHD centre for these patients,[23] widespread knowledge of these risk scores by general practitioners would help facilitate specialty referrals for patients with CHD who might be otherwise lost to specialty care.

Rather than developing a new risk prediction tool, we chose to evaluate the accuracy of existing pregnancy risk scores that already incorporate some important anatomical and functional considerations. Cardio-obstetric clinicians are already familiar with these existing risk scores and can easily incorporate data from this study to provide counselling regarding late cardiovascular events based on risk scores. Additionally, we found that a prepregnancy NYHA class is also a reliable predictor of late cardiovascular events; this is a simple tool that can easily be

ascertained via a thorough clinical history if a provider is not familiar with these cardiac risk scores.

Research implications

We found that NYHA class, CARPREG II score and ZAHARA score were predictive of late cardiac events in our single centre population of previously pregnant individuals with CHD. These findings should be confirmed in larger and multicentre longitudinal studies. Consideration should also be given to expanding our understanding in this area, including creation of a new risk prediction model specifically for late cardiac events following pregnancy. Additional research should focus on whether preconception counselling and targeted improvement of functional status can reduce the risk of late postpartum cardiac events. Given the finding that NYHA class was a strong predictor of late events, we hypothesise that improvement in prepregnancy NYHA class might help to improve long-term cardiovascular outcomes; more research is needed to support this. Other areas for future work include evaluating how multiple pregnancies affect risk, and whether pregnancy itself is associated with cardiac decline in patients with CHD by using a comparison group of never-pregnant patients with CHD.

Strengths and limitations

This study is limited by its retrospective nature, which limits data collection to what is available in the medical record. This design also limited the sample size of patients with available long-term follow-up, since many patients at our tertiary care institution return to community care after pregnancy and long-term outcomes are unknown. Similarly, adverse outcomes may have been underestimated since we did not have information regarding adverse outcomes that occurred at other facilities. This study is also subject to referral bias, as patients seen in our single tertiary centre may represent a more complex population of patients with CHD, thus limiting the generalisability of our findings. However, as more centres move towards this recommended model of multidisciplinary care for patients with complex cardiac conditions, our findings will become applicable to these institutions and populations.

Despite these limitations, this study provides contemporary data on the accuracy of existing pregnancy risk scores to predict late cardiovascular events among patients with CHD. This study is strengthened by its long postpartum follow-up time and by the use of manual chart extraction, which allows for more granular detail and accurate assessment of cardiovascular events compared with studies that use admission, billing, or administrative data.

CONCLUSIONS

Late cardiovascular events more than 6 months after delivery are common in patients with CHD. The ZAHARA and CARPREG II scores are useful in predicting these events, emphasising their utility in predicting not only peripartum cardiovascular events but also late maternal cardiovascular risks. Prepregnancy NYHA class is another simple, easy and reliable tool that can be used to predict late cardiovascular morbidity. These data provide important information for preconception counselling, risk modification and anticipation of adverse events late after pregnancy with CHD.

Acknowledgements The authors are thankful for the statistical input of Dr. Eric Vittinghoff, Professor of Epidemiology and Biostatistics at the School of Medicine, University of California, San Francisco, whose support was funded through the University.

Contributors HS: conceptualisation, investigation, formal analysis, original draft-writing, responsible for the overall content. NCS: conceptualisation, original draft-writing. SB: conceptualisation, formal analysis, review and editing. VY: data curation, visualisation JH: investigation. ISH: visualisation, resources, methodology. NP: conceptualisation, methodology. JG: supervision, review and editing. AA: conceptualisation, supervision, original draft-writing, review and editing, and responsible for the overall content as guarantor.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study was approved by the UCSF Committee on Human Research (Institutional Review Board #10-04360).

Provenance and peer review Not commissioned; internally peer reviewed.

Data availability statement Data are available on reasonable request. Data are available on reasonable request. Deidentified patient data are available through primary the primary author, ORCID 0000-0001-5787-2772, although reuse would be permitted only through researchers at the primary institution.

ORCID iDs

Hayley Schultz http://orcid.org/0000-0001-5787-2772
Vidhushei Yogeswaran http://orcid.org/0000-0001-6984-3602

REFERENCES

1 Gilboa SM, Devine OJ, Kucik JE, *et al*. Congenital heart defects in the United States: estimating the magnitude of the affected population in 2010. *Circulation* 2016;134:101–9.
2 Krasuski RA, Bashore TM. Congenital heart disease epidemiology in the United States. *Circulation* 2016;134:110–3.
3 Ouzounian JG, Elkayam U. Physiologic changes during normal pregnancy and delivery. *Cardiol Clin* 2012;30:317–29.
4 Elkayam U, Goland S, Pieper PG, *et al*. High-risk cardiac disease in pregnancy: Part I. *J Am Coll Cardiol* 2016;68:396–410.
5 Elkayam U, Goland S, Pieper PG, *et al*. High-risk cardiac disease in pregnancy Part II. *J Am Coll Cardiol* 2016;68:502–16.
6 Bowater SE, Selman TJ, Hudsmith LE, *et al*. Long-term outcome following pregnancy in women with a systemic right ventricle: is the deterioration due to pregnancy or a consequence of time? Congenit heart dis *Congenit Heart Dis* 2013;8:302–7.
7 Balint OH, Siu SC, Mason J, *et al*. Cardiac outcomes after pregnancy in women with congenital heart disease. *Heart* 2010;96:1656–61.
8 Siu SC, Sermer M, Colman JM, *et al*. Prospective multicenter study of pregnancy outcomes in women with heart disease. *Circulation* 2001;104:515–21.
9 Drenthen W, Boersma E, Balci A, *et al*. Predictors of pregnancy complications in women with congenital heart disease. *Eur Heart J* 2010;31:2124–32.
10 Silversides CK, Grewal J, Mason J, *et al*. Pregnancy outcomes in women with heart disease: the CARPREG II study. *J Am Coll Cardiol* 2018;71:2419–30.
11 Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, *et al*. 2018 ESC guidelines for the management of cardiovascular

diseases during pregnancy The task force for the management of cardiovascular diseases during pregnancy of the European Society of Cardiology (ESC). *Eur Heart J* 2018;39:3165–241.
12 Kim YY, Goldberg LA, Awh K, *et al*. Accuracy of risk prediction scores in pregnant women with congenital heart disease. *Congenit Heart Dis* 2019;14:470–8.
13 Harris PA, Taylor R, Thielke R, *et al*. Research electronic data capture (Redcap)–A metadata-driven methodology and workflow process for providing translational research Informatics support. *J Biomed Inform* 2009;42:377–81.
14 Marelli AJ, Mackie AS, Ionescu-Ittu R, *et al*. Congenital heart disease in the general population. *Circulation* 2007;115:163–72.
15 Schlichting LE, Insaf TZ, Zaidi AN, *et al*. Maternal comorbidities and complications of delivery in pregnant women with congenital heart disease. *J Am Coll Cardiol* 2019;73:2181–91.
16 Opotowsky AR, Siddiqi OK, D'Souza B, *et al*. Maternal cardiovascular events during childbirth among women with congenital heart disease. *Heart* 2012;98:145–51.
17 Lu C-W, Shih J-C, Chen S-Y, *et al*. Comparison of 3 risk estimation methods for predicting cardiac outcomes in pregnant women with congenital heart disease. *Circ J* 2015;79:1609–17.
18 Gatzoulis MA, Balaji S, Webber SA, *et al*. Risk factors for arrhythmia and sudden cardiac death late after repair of tetralogy of Fallot: a multicentre study. *Lancet* 2000;356:975–81.
19 Schwerzmann M, Salehian O, Harris L, *et al*. Ventricular arrhythmias and sudden death in adults after a mustard operation for transposition of the great arteries. *Eur Heart J* 2009;30:1873–9.
20 Ghai A, Harris L, Harrison DA, *et al*. Outcomes of late atrial tachyarrhythmias in adults after the Fontan operation. *J Am Coll Cardiol* 2001;37:585–92.
21 Agarwal A, Dudley CW, Nah G, *et al*. Clinical outcomes during admissions for heart failure among adults with congenital heart disease. *JAHA* 2019;8.
22 van Hagen IM, Boersma E, Johnson MR, *et al*. Global cardiac risk assessment in the Registry of pregnancy and cardiac disease: results of a registry from the European Society of Cardiology. *Eur J Heart Fail* 2016;18:523–33.
23 Stout KK, Daniels CJ, Aboulhosn JA, *et al*. 2018 AHA/ACC guideline for the management of adults with congenital heart disease: executive summary: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *Circulation* 2019;139:e637–97.