openheart

Pregnancy and cardiovascular outcomes among patients post Fontan surgery: a 25-year single-centre retrospective cohort study

Daniel Yehuda ,[1] Omri Soudry,[1] Eyal Schwartz,[1] Ilan Richter,[2] Alexander Dadashev,[2] Shahar Vig,[2] Shimon Kolker,[2] Ohad Houri,[1] Eran Hadar,[1] Ran Kornowski ,[2] Rafael Hirsch,[2] Nili Schamroth Pravda [2]

To cite: Yehuda D, Soudry O, Schwartz E, *et al*. Pregnancy and cardiovascular outcomes among patients post Fontan surgery: a 25-year single-centre retrospective cohort study. *Open Heart* 2025;**12**:e002843. doi:10.1136/openhrt-2024-002843

Received 6 August 2024
Accepted 5 December 2024

[1]Rabin Medical Center, Petah Tikva, Israel
[2]Department of Cardiology, Rabin Medical Center, Petah Tikva, Israel

Correspondence to
Dr Daniel Yehuda;
danielyehuda25@gmail.com

ABSTRACT

Introduction Data on the characteristics and outcomes of pregnancy and among patients with Fontan physiology are limited. We aimed to evaluate the immediate and long-term outcomes among these patients who were followed at our centre.

Methods We included adult patients who had undergone Fontan surgery for congenital heart disease and were pregnant between 1994 and 2021. We examined maternal and obstetric outcomes.

Results In a cohort of 109 patients following Fontan procedure, 51 patients were women, and 19 patients (37%) had a pregnancy during the follow-up period, accounting for a total of 46 pregnancies. Intrauterine growth retardation of the fetus was common, observed in 23% of all pregnancies and 50% of live births. The main fetal complication was prematurity, observed in 43% of all pregnancies and 90% of live birth. The maternal complications included pre-eclampsia (one patient), placental detachment (one patient), acute heart failure exacerbation (one patient), arrhythmia (three atrial arrhythmias) and major peripartum haemorrhage (two patients), with no peripartum death.

Conclusions Over one-third of women with Fontan physiology in our cohort had a documented pregnancy. Maternal and obstetric complications were common among these patients, and expanded long-term data is needed. Limitations, including small sample size and survival bias, may have underestimated the risk of adverse outcomes in this cohort.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Women with Fontan physiology face high maternal and fetal risks, yet specific data on these risks remain limited.

WHAT THIS STUDY ADDS

⇒ This real-world study highlights maternal and fetal complications in Fontan patients, including low fertility rates and increased risk of IUGR (Intrauterine growth retardation) and prematurity.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The study highlights the need for risk models and multidisciplinary management strategies for pregnant women with Fontan physiology. During pregnancy, cardio-obstetric teams should provide tailored counselling and risk assessment, based on the institution's experience, to ensure personalised recommendations aligned with local expertise.

INTRODUCTION

The prevalence of patients with congenital heart disease (CHD) surviving into adulthood is increasing due to medical and surgical advances.[1] The survival of children with CHD has increased substantially over the past decades, with 97% currently reaching adulthood.[2] With this increase in longevity, many patients are reaching childbearing age and have the desire to pursue pregnancy and childrearing. Pregnancy itself is a haemodynamic burden associated with blood volume loading, decreased systemic vascular resistance, and carries a circulatory burden.[3] This is true for women without cardiac conditions and has heightened repercussions for those with underlying pathologic cardiac conditions. Fontan surgery is the cumulation of a series of complex operations that allows for separation of the pulmonary and systemic circulations in patients with a single functioning ventricle.[4] Characteristics of the unique haemodynamics of the Fontan circulation include chronic systemic venous hypertension, non-pulsatile pulmonary blood flow and low cardiac output. The Fontan circulation is delicate and extremely susceptible to haemodynamic changes, such as those that occur during pregnancy. Pregnancy following the Fontan surgery is regarded as a high-risk medical scenario, with these patients regarded as mWHO III or mWHO IV

maternal cardiovascular risk as per European Society of Cardiology guidelines on cardiovascular disease during pregnancy.[5] Fontan patients with complications—such as patients with baseline saturations<85%, depressed ventricular function, moderate–severe atrioventricular valve regurgitation, refractory arrhythmia or protein-losing enteropathy—are regarded as mWHO Class IV maternal cardiovascular risk and the guidelines go as far as to recommend against pregnancy in these patients due to the high maternal risk during pregnancy.[5] This series of operations was initially described as palliative in nature. Current data suggest that over 80% of patients with Fontan circulation will reach adulthood.[6] Data on pregnancy outcomes in this population remain limited, with much of the available literature is based on small cohorts or registry data that may not fully capture real-world risks and outcomes. This study addresses this gap by providing a detailed assessment of maternal and fetal outcomes in a local cohort, offering insights to support more accurate, individualised preconception counselling and risk stratification for women with Fontan physiology who wish to pursue pregnancy.

METHODS

This study included women who had previously undergone Fontan surgery, had a documented pregnancy and were followed up at the Adult Congenital Heart Disease Clinic at Rabin Medical Center, Beilinson Hospital, between January 1994 and December 2021. Data was collected retrospectively. Detailed demographic and clinical data was extracted from patient files and electronic records; this included data from diagnostic tests, functional status as assessed by clinic physicians during follow-up visits, echocardiographic findings and interventional data. All patients managed at our centre are counselled at each visit on reproductive issues, including pregnancy conception, possible complications and recommendation according to guideline recommendations.[5]

Maternal complications during pregnancy included cardiovascular-related hospitalisation, arrhythmic events, decrease in left ventricular ejection fraction as assessed by echocardiography and all-cause mortality. All patients on chronic anticoagulation therapy were switched to weight-adjusted doses of low molecular weight heparin during pregnancy. Obstetric complications examined included preterm labour, miscarriage, adverse pregnancy outcomes and need for caesarean section operation. Pregnancies were defined according to gravity—the total number of times a woman was pregnant, regardless of the outcome of the pregnancy. Fetal outcomes included intrauterine growth retardation (IUGR) and low birth weight. Data on mortality were derived and adjudicated from the notification of death form legally required by the Israeli Ministry of Interior Affairs.

The primary outcome was a live birth versus miscarriage with the first pregnancy. Pregnancy outcomes were categorised based on the final status of each pregnancy, with live births defined as any pregnancy resulting in the birth of a viable infant. Miscarriages were defined as any pregnancy loss occurring ≤22 weeks of gestation. Additionally, adverse outcomes were documented for all pregnancies, including preterm births (classified as delivery before 37 weeks), intrauterine growth retardation and other complications based on clinical records and follow-up assessments. This outcome was taken to avoid the confounding nature of accessing outcomes from multiple pregnancies among different women.

Statistics

Baseline characteristics of the patients are presented by prior pregnancy status at last follow-up, as mean (SD)/median (IQR) for continuous variables, and count (%) for categorical variables as appropriate. Continuous variables were compared between groups using the student's t-test; categorical variables were compared using the $\chi 2$ test, as appropriate. All tests were two tailed, and a p value<0.05 was considered significant.

For the risk model of live birth versus miscarriage of first pregnancy, all non-missing variables (cut-off 90%) found to be associated with outcome in univariate analysis at a threshold of p≤0.25 were entered into a multivariable logistic regression model. Multicollinearity between included covariates was assessed using variance inflation factor. Model quality was assessed using Akaike's and Bayesian information criteria; model discrimination was assessed using the area under the receiver–operator curve, or c-statistic. Our small sample size was the deciding constraint in choosing our analysis approach. We favoured a whole-case, unmatched analysis to optimise power, while foregoing the employment of methods to control for confounding.

RESULTS

In a cohort of 107 patients following Fontan procedure, 51 patients were women. 19 patients (37%) of these women had 46 documented pregnancies during the follow-up period with 22 live births reported. One patient had ≥1 child via adoption and two women had ≥1 child via surrogacy.

Table 1 details the characteristics at last follow-up of these women who had a documented pregnancy. Among these women, the mean age at the time of Fontan was 9.5±7.3 years. None of the pregnant patients had severe complications of the Fontan circulation at the time of pregnancy (mWHO Class IV). The mean age at last follow-up or death was 38.0±6.0 years. Of these 19 patients, the average number of pregnancies among these patients was 2.3 (IQR 1–2.5) with an average of 1.1 live births (IQR 1–2). 11 patients (57.9%) had multiple pregnancies during the study period. The mean age at the time of first pregnancy was 28.7 years (IQR 26.3–30.7). The highest number of recorded live births in a single patient was three. The highest number of recorded pregnancies

Table 1 Characteristics of the cohort at last follow-up (n=19)

Age at last follow-up/death (years)	38 (±6)
Age at Fontan surgery (years)	9.5 (±7.30)
Time from Fontan surgery to last follow-up/death (years)	32 (24–35)
Fontan type	
Lateral tunnel	13 (68%)
Extra cardiac	4 (22%)
Bjork	1 (5%)
Atriopulmonary	1 (5%)
New York Heart Association Functional Class (NYHA) at last follow-up	
NYHA I–II	16 (84%)
NYHA III–IV	3 (16%)
Oxygen saturation (%)	93 (92–95)
Atrioventricular valve regurgitation	
None	5 (26%)
Mild	11 (58%)
Mild–moderate	3 (16%)
Systemic ventricle ejection fraction (EF)	
Preserved EF (>55%)	16 (84%)
Mildly reduced EF (40–50%)	3 (16%)
Reduced EF	0 (0%)
Aspirin	5 (26%)
Anticoagulation	10 (53%)
Atrial arrhythmia during pregnancy	3 (18%)
Pacemaker	2 (11%)
Cerebrovascular accident	4 (21%)

Data are presented as percentage, mean (SD) or median (IQR) as appropriate.

in a single patient was seven—in this patient only a single pregnancy resulted in a live birth.

IUGR of the fetus was common (11 pregnancies) in 24% of all pregnancies, and 50% among those with live births. The main fetal complication was prematurity (20 pregnancies) in 43% of all pregnancies, and 90% among those with a live birth. Of these pregnancies, three pregnancies had extreme prematurity (<28 weeks of pregnancy) and six were very preterm babies (between 28 and 32 weeks of pregnancy). The maternal complications included: pre-eclampsia (one patient), placental detachment (one patient) and major peripartum haemorrhage (two patients). Maternal cardiac complications during pregnancy included acute heart failure exacerbation (one patient) and arrhythmias (three atrial arrhythmias).

Nine patients were treated with low molecular weight heparin during pregnancy, seven with aspirin and one patient with both low molecular weight heparin and aspirin pharmacotherapy. There were no deaths in the peripartum period during follow-up, except for a single woman who died 18 years following her pregnancy. This woman developed protein losing enteropathy during pregnancy. Five women underwent caesarean section for different obstetric indications.

Table 2 shows a comparison of the primary outcome between live birth (n=13) and miscarriage (n=6) in the first pregnancy. Those with a miscarriage were significantly more likely to be older at last follow-up (42±5 vs 37±5 years, p=0.075) and to have had atrial arrhythmias (50% vs 0%, p=0.01).

DISCUSSION

The main findings of our cohort study are: first, over one-third of women with Fontan physiology in our cohort had a documented pregnancy; second, maternal and obstetric complications are common among these patients; third, almost half of these pregnancies cumulative in a live birth as shown in the central illustration (supplmentary figure 1).

The Fontan operation leads to a circulation in which there is chronic systemic venous hypertension, abnormal pulmonary perfusion and often reduced ventricular preload resulting in a chronically decreased cardiac output state.[7] This circulation is delicate and much more susceptible to the haemodynamic changes that occur in pregnancy. Various modifications have been made to this operation over the years, as shown in figure 1. The reported pregnancy outcomes are poorer, and fertility rates are decreased in this population as compared with that of the general population.[8] Our study is one of the first to report on fertility among a cohort of patients following Fontan surgery. The Australian New Zealand registry on this topic reported that only 27 of 157 women following Fontan surgery reported a pregnancy, and that fertility onset is delayed.[9] In contrast, almost one-third of women in our cohort had a pregnancy. Pregnancy and childbearing are a fundamental desire in the lives of many women. This is true despite the complexities and hazards of the Fontan circulation and potential pregnancy-related complications. In such, childbearing should be a topic that is discussed at all patient–physician consultations. Risk scores, specifically that of the ZAHARA Risk Score, have been derived from data among women with CHD.[10] These risk scores are important tools for preconception counselling and shared decision-making. These risk scores categorise patients according to their CHD and risk for a poor maternal outcome during pregnancy. However, Fontan pregnant patients are poorly represented in these scores and data on maternal–fetal outcomes of pregnancy in women with Fontan physiology are limited.[8 11] Our findings add to an increasing body of evidence on this topic and found that these women are at increased risk of maternal and fetal complications.[12] In our cohort, 40.9% of all pregnancies resulted in a live birth and there was a prominence of fetal adverse outcomes such as intrauterine growth retardation and prematurity. Importantly, in our

Table 2 Clinical parameters at last follow-up comparing women with primary outcome between live birth and miscarriage in the first pregnancy

	First pregnancy live birth, n=13	First pregnancy miscarriage, n=6	P value
Age at last follow-up or death (years)	37 (5)	42 (5)	0.075
Age at Fontan surgery (years)	10.35 (7.7)	7.6 (6.6)	0.50
Time from Fontan surgery to last follow-up or death (years)	28 (22–32)	35 (33–36)	0.011
Fontan type			
Lateral tunnel	10 (77%)	2 (33.3 %)	0.125
Extra cardiac	3 (23 %)	2 (33.3%)	
Bjork	0 (0%)	1 (16.6 %)	
Atriopulmonary	0 (0%)	1 (16.6%)	
New York Heart Association Functional Class (NYHA) at last follow-up			
NYHA I–II	11 (85%)	5 (83%)	0.94
NYHA III–IV	2 (15%)	1 (17%)	
Oxygen saturation (%)	93 (92–95)	92 (83–93)	0.10
Atrioventricular valve regurgitation			
None	3 (27%)	1 (17%)	0.87
Mild	6 (55%)	4 (67%)	
Mild–Moderate	2 (18%)	1 (17%)	
Systemic ventricle ejection fraction (EF)			
Preserved EF	11 (85%)	5 (83%)	0.94
Mildly reduced EF	2 (15%)	1 (17%)	
Atrial arrhythmia during pregnancy	0 (0%)	3 (50%)	0.01
Prior cerebrovascular accident	2 (15%)	2 (33%)	0.37
Heart failure hospitalisation	1 (8%)	1 (17%)	0.60

Data are presented as percentage, mean (SD) or median (IQR) as appropriate.

cohort, prematurity was a complication in 90% of all live births. Our findings are additive to previous studies that reported a high risk of fetal loss of up to 55%, and fetal complications such as intrauterine growth retardation and prematurity in this unique population.[13] The aetiology of this finding is multifactorial. There is evidence to suggest a degree of placental insufficiency among these women.[14] The main cause may be the haemodynamic status of the Fontan circulation itself, with reduced preload and limited cardiac output. This circulation is stressed at baseline functioning, is strained further during pregnancy and may not be

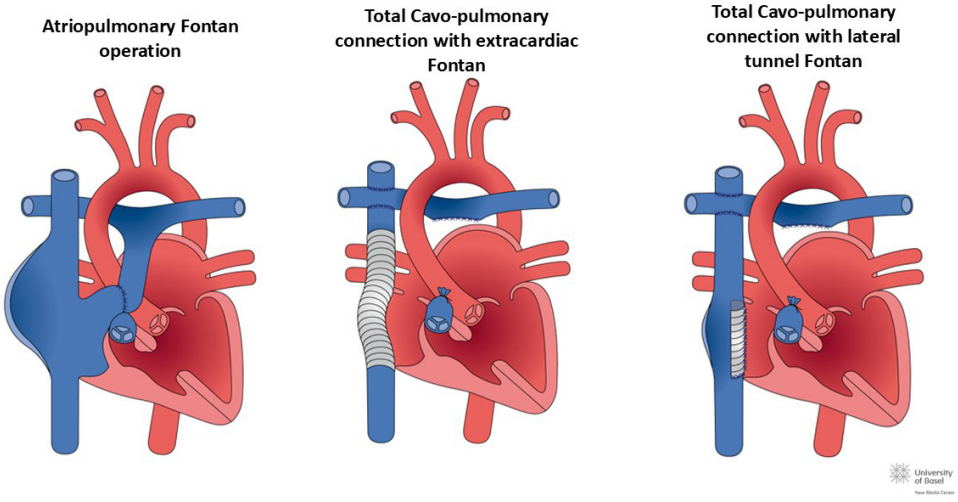

Figure 1 Three types of Fontan operation for tricuspid atresia. Illustration taken from http://www.chd-diagrams.com.

optimal for maintaining fetal growth. Treating physicians should be aware of this with increasing follow-up towards delivery, during which further haemodynamic changes occur and ensure the patient is planned for a delivery at a tertiary centre with adequate resources for mother and baby.

Our findings of atrial arrhythmias complicating a pregnancy in Fontan women have been reported in other cohorts. This is most likely due to the increased blood volume during pregnancy and increased atrial stretch and stress. This is congruent with a review from Garcia Ropero *et al* that investigated clinical outcomes from live births among Fontan pregnant patients, among them higher maternal morbidity was shown including atrial arrhythmias, pregnancy-related bleeding and heart failure.[8]

Importantly, none of the women in our cohort died peripartum or during the year following pregnancy. All pregnancies in women with Fontan physiology are regarded as high-risk pregnancies. According to the mWHO classification of maternal morbidity and mortality in pregnancy, patients with a well-functioning Fontan circulation have a cardiac event rate of 19–27% during pregnancy and are advised to have bimonthly/monthly follow-up during pregnancy at an expert centre.[5] Those with Fontan with any complication classify as extremely high risk of maternal mortality or severe morbidity (40–100% cardiac event rate, ie mWHO Class IV) and the guidelines suggest preconception counselling to avoid pregnancy, and for monthly follow-up at an expert centre in the case of a desired pregnancy.[13] All our patients who were pregnant were mWHO Class III. The under-representation of those in mWHO Class IV could be that these patients adhered to counselling to avoid pregnancy or that these women are at increased risk of early spontaneous miscarriages, which may not have been reported. We did report that three patients opted for adoption/surrogacy according to our recommendation to avoid pregnancy and potential complications.

Those with a miscarriage in the first pregnancy were significantly more likely to be older at last follow-up (42±5 vs 37±5 years, p=0.075) and to have had an atrial arrhythmia (50% vs 0%, p=0.010). The explanation for the increased rate of miscarriage in those with older age in our cohort is multifactorial. This may be reflective of the dampened reproductive status in older women and may also be reflective of the decreasing functioning of the Fontan circulation in older women with less reserve to support pregnancy. As discussed above, atrial arrhythmias are commonly reported during pregnancy in this population.[8]

Clinical implications

This study highlights the significant risks faced by pregnant women with Fontan physiology, and addressing these requires a comprehensive, multidisciplinary approach. Prepregnancy clinical assessment, including imaging and functional testing, is crucial to establish a baseline and anticipate complications. Preconception counselling, incorporating risk tools, helps guide discussions on pregnancy risks and alternatives such as surrogacy or adoption. Managing these patients requires a cardio-obstetrics team for close monitoring, personalised delivery planning, and careful postpartum follow-up to manage complications such as heart failure and arrhythmias. Anticoagulation and arrhythmia management, particularly in the third trimester and postpartum, are key to optimising maternal and fetal outcomes.[15] This approach helps tailor care and improve decision-making for this high-risk population.

Our data have some important limitations. The study cohort consists of adult women who have survived

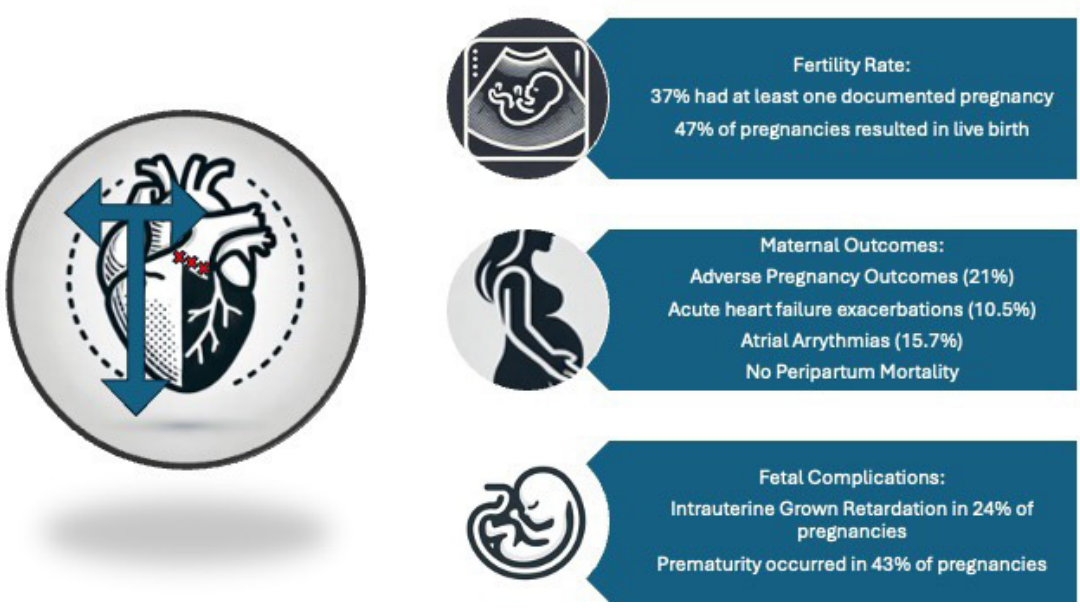

Figure 2 Maternal and Fetal outcomes.

long enough post Fontan surgery to become pregnant, introducing survival bias. As a result, the cohort might disproportionately reflect women with relatively better-functioning Fontan physiology, potentially leading to an underestimation of maternal and fetal risks. Due to the retrospective nature of this project, some of the patient files had missing data and some complications may have occurred prior to electronic documentation and thus not included in our analysis. However, each patient file was reviewed by two clinicians to ensure complete data collection. The number of patients in this cohort was small. This limited the power of the study to detect associations or differences between subgroups such as type of Fontan, age of surgery or Fontan-associated complications. Longer-term follow-up is needed to assess whether pregnancy has lasting effects on the cardiac function of women with Fontan physiology and to guide long-term management strategies post pregnancy These factors may limit the generalisability of our findings to other populations or centres, underscoring the need for larger, prospective studies to validate these results in broader and more diverse cohorts.

In conclusion, our real-world findings show low fertility rates and a high incidence of intrauterine growth retardation and prematurity among women following Fontan surgery. The maternal pregnancy outcomes are not only encouraging but also highlight the need for specialised multidisciplinary care in this situation. Further data are needed on this important topic.

This study contributes to the growing body of knowledge on pregnancy risks in women with Fontan physiology, highlighting significant maternal and fetal complications and underscoring the challenges these patients face. By providing real-world data from a local cohort, our findings help tailor informed counselling and management in this unique population. Future research should focus on multicentre studies and prospective cohort designs to enhance the generalisability of findings and refine risk assessment tools Figure 2.

Contributors DY: Guarantor; conception or design of the work; acquisition, analysis, drafting the work and reviewing; final approval of the version to be published. OS, ES, AD, SV, SK, OH and EH: Acquisition of data for the work; drafting the work and reviewing; final approval of the version to be published. IR: Analysis and interpretation of data for the work; drafting the work and reviewing; final approval of the version to be published. RK: Supervision; drafting the work and reviewing; final approval of the version to be published. RH: Conception of the work; drafting the work and reviewing; final approval of the version. NRSP: Conception of the work; supervision, the acquisition, analysis of data for the work; drafting the work and reviewing; final approval of the version. AI technology (ChatGPT 4.0) was used to create unique icons used in the central illustration.

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 received ethics board approval from the Rabin Medical Center institutional committee. (approval number RMC 780-22) and was conducted in accordance with the Declaration of Helsinki guidelines on research involving human subjects. Informed consent was waived due to the retrospective nature of the study.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. All data were securely stored, anonymised and accessible only to the research team to ensure patient confidentiality and compliance with data protection regulations.

ORCID iDs
Daniel Yehuda http://orcid.org/0009-0006-8143-3626
Ran Kornowski http://orcid.org/0000-0002-7708-8253
Nili Schamroth Pravda http://orcid.org/0000-0002-0989-187X

REFERENCES

1 Moons P, Bovijn L, Budts W, *et al*. Temporal trends in survival to adulthood among patients born with congenital heart disease from 1970 to 1992 in Belgium. *Circulation* 2010;122:2264–72.
2 Dellborg M, Giang KW, Eriksson P, *et al*. Adults With Congenital Heart Disease: Trends in Event-Free Survival Past Middle Age. *Circulation* 2023;147:930–8.
3 Davis MB, Arendt K, Bello NA, *et al*. Team-Based Care of Women With Cardiovascular Disease From Pre-Conception Through Pregnancy and Postpartum: JACC Focus Seminar 1/5. *J Am Coll Cardiol* 2021;77:1763–77.
4 Rychik J, Atz AM, Celermajer DS, *et al*. Evaluation and Management of the Child and Adult With Fontan Circulation: A Scientific Statement From the American Heart Association. *Circulation* 2019;140:e234–84.
5 Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, *et al*. 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy. *Eur Heart J* 2018;39:3165–241.
6 Poh CL, d'Udekem Y. Life After Surviving Fontan Surgery: A Meta-Analysis of the Incidence and Predictors of Late Death. *Heart Lung Circ* 2018;27:552–9.
7 Kverneland LS, Kramer P, Ovroutski S. Five decades of the Fontan operation: A systematic review of international reports on outcomes after univentricular palliation. *Congenit Heart Dis* 2018;13:181–93.
8 Garcia Ropero A, Baskar S, Roos Hesselink JW, *et al*. Pregnancy in Women With a Fontan Circulation: A Systematic Review of the Literature. *Circ Cardiovasc Qual Outcomes* 2018;11:e004575.
9 Zentner D, Kotevski A, King I, *et al*. Fertility and pregnancy in the Fontan population. *Int J Cardiol* 2016;208:97–101.
10 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.
11 Cauldwell M, Steer PJ, Bonner S, *et al*. Retrospective UK multicentre study of the pregnancy outcomes of women with a Fontan repair. *Heart* 2018;104:401–6.
12 Sobhani NC, Corbetta-Rastelli CM, Agarwal A, *et al*. Delivery trends and obstetric outcomes in patients with Fontan circulation. *Am J Obstet Gynecol MFM* 2023;5:100921.
13 Baumgartner H, De Backer J, Babu-Narayan SV, *et al*. 2020 ESC Guidelines for the management of adult congenital heart disease. *Eur Heart J* 2021;42:563–645.
14 Phillips AL, Cetta F, Kerr SE, *et al*. The placenta: A site of end-organ damage after Fontan operation. A case series. *Int J Cardiol* 2019;289:52–5.
15 Montanaro C, Boyle S, Wander G, *et al*. Pregnancy in patients with the Fontan operation. *Eur J Prev Cardiol* 2024;31:1336–44.