Fontan circulation and implications for future reproduction

Niharika Mehta^{1,2} and Srilakshmi Mitta^{1,2}

Abstract

This article summarizes and critiques four recent publications looking at preconception counseling, pregnancy outcomes, and cardiac complications in women with history of Fontan circulation. The Fontan procedure is a palliative strategy for single-ventricle type congenital heart disease and involves passive flow of venous return into the pulmonary circulation, bypassing the ventricles. Pregnancy in these patients is not without risk and preconception counseling and contraception practices vary widely. High rates of miscarriage, prematurity, and small-for-gestational-age babies are reported. Cardiac complications include mainly arrhythmias. Whether long-term prognosis in these patients is affected by pregnancy is not yet known.

Keywords

Cardiovascular, maternal–fetal medicine, high-risk pregnancy, physiology

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Introduction

The Fontan operation is a palliative strategy for children born with single-ventricle type of congenital heart disease. It involves channeling systemic venous return directly to the pulmonary circulation without the need for a ventricular pump to propel blood into pulmonary vasculature. Since its introduction in the 1970s, survival has improved dramatically. However, the procedure is not without long-term sequelae. Patients with Fontan circulation have an increased risk of ventricular failure, thromboembolism, arrhythmias, liver fibrosis, and protein-losing enteropathy (PLE).¹

Absence of ventricular thrust and passive cavo-pulmonary flow after Fontan operation leads to a relatively low cardiac output state in comparison to normal. Some consider the Fontan state to be one of chronic ventricular volume depletion,² where patients are unable to adequately increase stroke volume during periods of increased demand.³ Do such patients then tolerate pregnancy? Historically, women with Fontan circulation were advised to refrain from pregnancy. Are they then adequately counseled regarding contraception and pregnancy risks? What do we know about their reproductive choices? For women who do get pregnant, how well is pregnancy tolerated and what are the pregnancy outcomes?

The following four papers published in the last year may help to answer some of these questions.

Fertility and pregnancy in the Fontan Population

Zentner D, Kotevski A, King I, et al. *Int J Cardiol* 2016; 208: 97–101

This was a registry-based cross-sectional study, exploring fertility and pregnancy data in the Fontan population. All women ≥ 18 years of age, in the Australian & New Zealand Fontan Registry, who had consented to being approached regarding research projects at time of registry enrollment, were included. Of 152 women who were contacted, 97 (64%) completed the initial survey. The survey contained questions regarding gynecologic history, baseline cardiac disease and surgical history, current contraceptive use and medications, as well as pregnancy and preconception counseling. When applicable, registry data on those women who were deceased or refused participation were used for comparison.

The most common method of contraception was the combined oral contraceptive pill (COCP) (22%). Other forms of contraception included condoms (8%), minipill (11%), progestin-only implant

(11%), and intrauterine devices (4%). A total of 37 women (38%) had either never used contraception or were using nothing.

Most women acknowledged receiving preconception counseling. Only 6% said they were given no advice at all, 12% were told pregnancy was associated with no risk or only a slightly increased risk, 55% were told that pregnancy would be inadvisable or had a significantly increased risk, and 26% were advised not to get pregnant.

A total of 27 women (28%) reported pregnancies. Of those, 23 had previously been informed of risk or cautioned against pregnancy.

Details on 40 pregnancies in 20 women were available. Thirty-two pregnancies (80%) were natural conceptions, and seven conceived with ovarian induction. There were 17 miscarriages (43%) and 16 pregnancies that went beyond 20 weeks gestation with an average age at delivery of 31 weeks and two neonatal deaths. No maternal complications were noted in 6 of the 14 pregnancies that resulted in livebirths.

The most common complication was antepartum or postpartum bleeding (71%), but it is noteworthy that 79% of women were treated with either aspirin or a combination of low molecular weight heparin (LMWH) with or without warfarin during pregnancy. Only one delivery was complicated by postpartum heart failure and there were no maternal deaths.

This study touches on some of the challenges faced in care of women with Fontan circulation. The authors address the issue of increased thromboembolic risk in Fontan patients; yet, COCP is often prescribed in this population. In this cohort, patients were more often than not advised regarding pregnancy risks, but pregnancy complications of miscarriage and preterm births were high with livebirth resulting in only 40%. Limitations to this study include the known downsides to a cross-sectional study—namely that it is looking only at one point in time and also contains recall and selection bias. The low number of surveys returned also limited the strength of the study.

¹Department of Medicine, Warren Alpert Medical School of Brown University, Providence, RI, USA

²Division of Obstetric Medicine, Women and Infants Hospital of Rhode Island, Providence, RI, USA

Corresponding author:

Niharika Mehta, Department of Medicine, Warren Alpert Medical School of Brown University, Box G-A1, Providence, RI 02912, USA.

Email: nmehta@wihri.org

A cohort study of women with Fontan circulation undergoing preconception counseling

Cauldwell M, Von Klemperer K, Uebing A, et al. *Heart* 2016; 102(7): 534–540

This retrospective study from an academic institution in the United Kingdom, focusing on patients who were given preconception counseling at a multidisciplinary cardiac pregnancy service, explored the impact of counseling on the decision to become pregnant, pregnancy rates, and short- and long-term outcomes of those who did achieve a successful pregnancy. Women with Fontan circulation, aged between 16 and 45 years who attended Preconception counseling (PCC) were included. After preconception counseling, the choices made by patients were recorded: (1) avoid pregnancy, (2) attempt to become pregnant, or (3) delay attempting to become pregnant. Records were reviewed from 1994 to 2014 to determine initial health status and subsequent health and pregnancy outcomes. The outcomes were grouped in maternal, neonatal, and obstetric outcomes. Cardiac disease in pregnancy (CARPREG) scores were calculated as they have been validated in assessing maternal cardiovascular risk. For each pregnancy in a patient with Fontan, two normal controls were identified, delivering just before and just after the index case, to account for changes in demographics and practice over time. Fifty women who were offered preconception counseling were included in the study. Following PCC, 19 women decided to try to conceive, 15 decided not to pursue pregnancy, and 16 confirmed they wished to consider pregnancy in future. Comparing women who chose to conceive against those who chose to avoid pregnancy, CARPREG scores, rates of hypoxia, and history of arrhythmia were similar. In contrast, those who chose to defer pregnancy had better CARPREG scores and lower incidence of hypoxia. The authors discuss that these data imply that factors other than severity of disease may be of importance to women in their reproductive decisions.

Among women who conceived, CARPREG scores were better and hypoxia rate was lower in the group who carried at least one pregnancy to viability versus the group who only had miscarriages, suggesting CARPREG scores can be a risk-assessment tool prior to pregnancy. Eight women had a total of 14 livebirths and nine miscarriages. Preterm delivery and small-for-gestational-age (SGA) babies were common. There was one neonatal death in a preterm baby born at 32 weeks gestation. Cardiovascular complications, mainly atrial arrhythmias occurred in five pregnancies. One patient developed pulmonary embolism postpartum.

This series confirms the association between Fontan circulation and increased risk of miscarriages and preterm delivery. The risk of SGA in this series (57%) was double that of general congenital heart disease population as reported previously by the same group.⁴ In women who were hypoxic, these risks were higher and chance of successful pregnancy was lower.

The study was limited by its retrospective nature and small sample size. In addition, there were no patients in the study group who were New York Heart Association (NYHA) class 3 or 4 or who were known to have PLE. At this institution, all patients with Fontan circulation were treated with thromboprophylaxis routinely. Whether this had any impact on the low incidence of Venous thromboembolism (VTE) is unknown. It is also noteworthy that this study utilized CARPREG scores for risk assessment, whereas several recent publications have reported overestimation of risk with this tool.^{5,6} The authors conclude that among women with Fontan circulation, choices regarding pregnancy are multifactorial; rates of miscarriage are high and correlate with maternal hypoxia.

Contraception practices and pregnancy outcome in patients after Fontan operation

Pundi KN, Pundi K, Johnson JN, et al. *Congenit Heart Dis* 2016; 11: 63–70

This single-center retrospective study from a tertiary care health center in the United States, aimed to determine contraception practices and early and late pregnancy outcomes after Fontan procedure. Records of all patients who had an initial Fontan operation at the Mayo Clinic or other institutions with subsequent follow up at the Mayo Clinic were identified. Between 31 October 1973 and 30 June 2012, 455 women underwent Fontan procedure at Mayo clinic. Of these, 167 women were known to be deceased at time of the study. Data regarding contraception practices and pregnancies were ascertained by reviewing Mayo clinic medical record and medical questionnaires sent to patients. A total of 138 completed questionnaires with available contraception and/or pregnancy data were received. Of the 138 women, 44% ($n=61$) used no contraception; 12% used barrier methods, combination hormone therapy, or sterilization; 8% used Depo-Provera; 7% had intrauterine devices; 4% had partners with vasectomy; and 1% used progestin-only pills. Incidence of venous thromboembolism was not different in the patients with and without contraceptive use. Of these, 49 acknowledged that at least one physician had counseled them to avoid pregnancy.

Pregnancy data were available for 35 women: 10 pregnancies occurred prior to Fontan procedure (eight miscarriages, two terminations), 70 pregnancies occurred after Fontan operation, resulting in 35 miscarriages (50%), 29 livebirths, and six therapeutic abortions. The spontaneous miscarriage rate of 50% was consistent with prior reports.^{7,8} Preterm delivery was common (81%) and there was one neonatal death from extreme prematurity.

No viable pregnancies occurred in women with resting oxygen saturations less than 90%. In long-term follow-up (mean 13.3 years $\pm$ 4.7 years since first pregnancy), multiparous patients with live born children ($n=7$) did not show progressive decline in ventricular systolic function with successive pregnancies. There were no maternal deaths during pregnancy. Among 19 women with 29 livebirths, atrial arrhythmias were noted in 32% of women, who managed successfully with oral medications or electrical cardioversion. No thromboembolism was noted although 14 of 19 patients were treated with some form of anticoagulation, either aspirin or heparin. Delivery information was available for 14 women: 71% had Cesarean sections and 29% had vaginal deliveries with no information about complications.

The authors conclude that despite anecdotal data about successful pregnancy after Fontan procedure, it is important to counsel women about risks of miscarriage, prematurity, and low birthweight. They acknowledge the limitation that much of the collected data were from surveys and subject to selection and recall bias.

Maternal and fetal outcomes of pregnancy with Fontan circulation: A multicentric observational study

Gouton M, Nizard J, Patel M, et al. *Int J Cardiol* 2015; 187: 84–89

This was a multicenter, retrospective study including 37 women with a total of 59 pregnancies, who were registered between 2000 and 2014 at 13 different congenital cardiac disease centers throughout France. The study was conducted to determine maternal and fetal outcomes of pregnancy in women with a Fontan circulation as well as the impact of pregnancy on heart disease. Data regarding their initial cardiac anatomy, surgeries and subsequent cardiac complications, baseline gynecologic/obstetric history, and pregnancy and postpartum were collected. Complications were divided into categories—maternal cardiac, obstetrical, and neonatal.

At baseline, the age at first pregnancy was 27 ± 5 years, and age at Fontan palliation was 13 ± 7 years. There were no women in NYHA class 3 or 4 functional state. Most women (89%) had normal systemic ventricular function, and no women had severe dysfunction. Seven women (19%) had a baseline arrhythmia.

Cardiovascular complications during pregnancy included six women with cardiac events (10%): Supraventricular tachycardia (SVT), systemic VTE, and heart failure. Of the patients with an atrial arrhythmia, a past medical history of arrhythmia was highly

predictive with an odds ratio of 18.3%. There were no ventricular arrhythmias noted. There were three women with thromboembolic events, of which two were not on any anticoagulation. Heart failure occurred in three patients postpartum and there was no maternal mortality. Obstetrical and neonatal outcomes were significant for miscarriages in 16 women (27%), 25 babies were born premature (69%) with 22 vaginal deliveries (58%) and 16 Cesarean deliveries (42%). Finally at a median of 24 months follow-up, a total of eight women (22%) experienced a cardiac event (arrhythmia, pacemaker placement, and stroke).

The authors discuss that the high rate of miscarriage is twice that of congenital cardiac patients⁹ and three times the rate in general population.¹⁰ Prematurity was common (69%). Maternal cardiac complications were primarily arrhythmias, especially in those with preexisting history. Limitations to this study are that it is a retrospective study looking at many centers that do not share standardization of treatment, management, or follow-up. Selection bias toward more healthy patients, that is, those who would have been counseled that it was okay to get pregnant, was also likely.

Conclusion

In summary, data from different regions across the world suggest that pregnancy in Fontan circulation is not without risk. Despite preconception counseling, only half the women admitted to using some form of birth control. Pregnancy, when it does occur is not without maternal and fetal risk. High rates of miscarriage, prematurity, and SGA babies are reported. Cardiovascular complications noted are mainly atrial arrhythmias. Prepregnancy functional capacity is an important indicator of outcome. Data regarding long-term effects of pregnancy on Fontan patients is unknown. Further studies characterizing thrombotic risk during pregnancy in these patients and long-term prognosis after pregnancy will empower informed preconception counseling and guide appropriate management during and after pregnancy.

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