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Fertility and pregnancy in the Fontan population☆

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ABSTRACT

Background: Women with a Fontan circulation are deemed at significantly increased risk of maternal morbidity and mortality during pregnancy. Publications describe a small number of pregnancies worldwide and a high rate of miscarriage. We compiled the experience of women enrolled in the Australia and New Zealand Fontan (ANZ) Registry with regard to menarche, contraceptive use, pregnancy advice and pregnancy outcomes.
Methods: Women within the ANZ Fontan Registry were contacted and asked to consent to receiving sequential questionnaires.
Results: 156 women ≥18 years of age (including 4 deceased individuals) were identified, 101 women consented and 97 completed the initial questionnaire. Women were aged (median) 25 years (23–32); menarche occurred at a median 14 years (13–16). A wide variety of contraceptive methods was reported. 81% of women reported having received advice that pregnancy carried an increased risk or was inadvisable. Pregnancy was reported in a minority (n = 27). Miscarriage (42.5%) and termination (7.5%) accounted for half the pregnancy outcomes and the babies were born early (median 31.5 weeks) and small (median 1350 g). Maternal complications of bleeding, arrhythmia and heart failure were reported with no early maternal mortality.
Conclusions: In women with a Fontan circulation the fertility onset is delayed and pregnancy has a higher rate of miscarriage. Successful pregnancy resulted in small and premature babies. Significant maternal morbidity occurred. Whether pregnancy with its volume loading has an adverse effect on the long-term outcome of women with a single ventricle remains to be elucidated.

1. Introduction

A Fontan circulation represents the final common pathway for a number of complex cardiac congenital conditions and is unique for relying on a passive circulation where central venous pressure drives pulmonary blood flow and, consequently, cardiac output [1]. Unfortunately, even the pioneer of the procedure recognised its limitations stating, more than 20 years ago, that it "imposes a gradually declining functional capacity and premature late death after an initial period of often excellent palliation" [2]. Although this data pertain to outcomes of the early atriopulmonary connection approach and the surgical technique has since been revised, follow-up data suggests ongoing significant morbidity in this population [3]. In 2008, the Australia and New Zealand (ANZ) Fontan Registry was created in order to collect data on all children and adults with a Fontan circulation in these two countries. The aims of the study were to establish current cross sectional data on menstrual history, contraceptive use, medication and anticoagulation use as well as reported medical advice regarding pregnancy. If women had undergone a pregnancy, further information regarding complications and outcomes was sought, as possible.

Pregnancy is a physiological challenge and has been shown to cause measureable asymptomatic decrease in cardiac function [4] as well as appearing to contribute to worse clinical outcomes in a number of different cardiac pathologies [5–7]. The AHA Guidelines for Adults with Congenital Heart Disease have a Class I recommendation that all women with a Fontan operation need a comprehensive evaluation prior to proceeding with pregnancy, by a physician experienced in adult congenital heart disease (ACHD) [8]. The European Society of Cardiology Guidelines states that successful pregnancy is possible in selected patients with intensive monitoring [9]. The 2011 ESC Guidelines on the management of cardiovascular disease in pregnancy classify the Fontan circulation as WHO III for pregnancy risk; meaning that there is a significantly increased risk of maternal mortality or severe morbidity [10].

Additionally, the Fontan population is usually mildly cyanosed, a physiological state that may decrease fertility and results in more miscarriages [11,12]. Warfarin is often prescribed as an anticoagulant, adding to the challenges of pregnancy management. Choice of

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contraceptive method needs to be balanced against the risks of contraceptive method failure and potential pregnancy. Pregnancy, if attained, appears to usually result in the premature delivery of a small-for-age baby. Maternal cardiac status can also be compromised, most commonly due to arrhythmias, but also secondary to deterioration in cardiac function [13].

Current data, worldwide, is small but suggests approximately a 50% pregnancy completion rate in this population [10].

We chose to explore fertility and pregnancy data within a Fontan population further via a series of questionnaire studies.

2. Methods

The Australian and New Zealand Fontan Registry (Fontan Registry) collects a limited number of health data in all children and adults who have survived a Fontan operation in Australia and New Zealand [14]. At enrolment, all participants are asked to consent to being approached regarding research projects that are supported by the governance committee. We obtained Ethics approval (HREC 2011.270) to approach all women ≥18 years of age who had self consented to Registry inclusion and agreed to be further contacted regarding research (n = 152). During the time of this study the Fontan Registry independently obtained ethics approval for automatic inclusion of deceased individuals. There were subsequently 4 deceased women in the ≥18 years of age group included in the Registry, bringing the total population of women ≥18 to 156.

Contact was attempted with the 152 women. A cohort of 101 (66%) women consented of whom 97 (64%) filled in the initial questionnaire. Of the remaining women, 12 (8%) refused participation and 1 withdrew after giving consent. There were 7 lost to follow-up/where mail was returned to sender (4.6%). The remaining 31 (20%) did not respond despite repeated attempts at contact (mail, email and telephone as available). Data is presented for the women who consented. Additionally, baseline registry data on the 17 women who were deceased or refused participation was reported with respect to demographic, anatomical and surgical data, as available, to determine whether they differed from the rest of the population.

3. Statistical methods

Participant entered data was transferred from the questionnaires into an excel sheet and subsequently into SPSS V22 for analysis. All data is described as median and interquartile range.

4. Results

4.1. Demographics

Fontan surgery was performed at a median age of 4.9 years (3.2–9.2). At the time of the first questionnaire, women were a median of 21 years (18–24) post Fontan surgery with a median age of 25 years (23–32). Patients' characteristics are listed in Table 1. The deceased women had undergone Fontan operation at an older age (median 6.8 years, no IQR calculated given small numbers). There was no data available on the operative age in the women who declined to participate.

Women who were either deceased or refused/withdrew from the study did not appear to be different apart from being slightly younger.

4.2. Menarche and contraception

Our cohort of women reports a median age at menarche of 14 years (13–16) and have utilised a number of different contraceptive methods (Table 2). Contraceptive use (both ever and current) is described in Table 2.

4.3. Current anticoagulant and medication use

Table 3 describes current medication usage. Most of the women in this cohort are on antiplatelet or anti-thrombotic medications (85/97, 88%). The majority report anticoagulation with warfarin (60%) as opposed to the use of aspirin (27%). Details on other medications were additionally available in the 4 women who consented but did not respond to the questionnaire (total n = 101).

4.4. Pregnancy advice

Women were asked to explain the pregnancy advice they had been given. Some women reported different advice being given and thus a combined category between options has been created to capture their individual experiences (Table 4).

4.5. Pregnancy outcomes

Within our cohort, 27 women reported pregnancy, with details provided on 40 pregnancies in 20 women, including 1 twin pregnancy. 68 women reported never having had a pregnancy. Two women declined to respond as to whether they had ever had a pregnancy. Of the pregnancies, there were 15 babies discharged home (38%) (Table 5).

In the 27 women reporting pregnancy, the spread of medical advice given appeared similar to the overall population. They reported; no advice (n = 1), that pregnancy would be all right (n = 3), that pregnancy was at increased risk (n = 15), that pregnancy was at increased risk *to* inadvisable (n = 2) and that pregnancy was inadvisable (n = 6).

The median number of pregnancies per woman was 2 (1–2.5), ranging from 1 to 6. Further details are provided in Table 5.

4.6. Maternal pregnancy outcomes

Details about maternal health were available from 11 women who had undergone a total of 23 pregnancies. These resulted in: 14 births with 15 babies (1 twin pregnancy) and 9 miscarriages. Unfortunately, 1 birth was a stillbirth and there were 2 early neonatal deaths due to prematurity.

Table 1
Original cardiac morphology and Fontan operation type.

Morphology and surgical details (n = 101)	AP (n = 39, 40%)	LT (n = 52, 52%)	ECC (n = 10, 8%)	Total with known morphology n/%
Tricuspid atresia	15[a]	15	0	30
Corrected transposition of the great arteries	2	4	3	9
Double-inlet left ventricle	12	13	1	26
Double-outlet right ventricle	5	10	2	17
Complete atrioventricular canal defect	0	2	1	3
Pulmonary atresia with intact ventricular septum	2	3	0	5
Hypoplastic left heart syndrome	0	0	1	1
Other	3[a]	5	2	10

This table shows the spread of different primary cardiac morphology diagnoses and type of Fontan surgery undertaken in the participants. AP = atriopulmonary, LT = lateral tunnel and ECC = extracardiac connection.

[a] 1 patient subsequently underwent a Fontan conversion with an ECC.