Pregnancy in a woman with a Fontan circulation: A review

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Abstract

More women with congenital heart disease survive to childbearing ages, due to improvements in surgical practice and postoperative care. This review discusses pregnancy in women with a single ventricle, describing maternal obstetric and cardiovascular complications and the increased risks of prematurity and adverse neonatal outcomes. Recommendations are made based on current understanding, guidelines and published literature, with recognition that there is much knowledge yet to be gained.

Keywords

Heart defects, congenital, pregnancy complications, arrhythmias, cardiac, heart failure, Fontan circulation

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Overview

The Fontan procedure is performed in individuals with a single ventricle, bypassing the usual flow of systemic blood to the heart. This procedure is now the destination operation in congenital heart defects (CHDs) unable to sustain biventricular anatomy. Unlike a biventricular circulation, blood flow into the pulmonary arteries is passive with no intervening pump. This results in systemic venous congestion and limited capacity to increase cardiac output.¹

This physiology is further challenged by pregnancy, with its described increases in plasma volume and cardiac output.^{2,3} In the developed world, maternal cardiovascular disease is the major cause of pregnancy-related maternal death.^{4,5} Pregnancy may lead to worse outcomes in women with cardiac conditions^{6,7} and may cause measurable reductions in the normal functioning of women.^{8,9} Women with significant cardiac pathology are best cared during pregnancy by a multidisciplinary approach, in experienced specialised centres, encompassing both the pre-conception and postpartum phase.

Preconception counselling and assessment

Ideally, contraception and pregnancy discussions should be initiated prior to conception and during teenage years.¹⁰ The 2011 European Society of Cardiology Guidelines classify pregnancy for women with a Fontan circulation as at moderate to high risk of maternal morbidity and mortality risk (World Health Organization (WHO) risk class III–IV).¹¹ This is based on the Fontan circulation (Class III) and changes to Class IV if there is significant systemic ventricular dysfunction or heart failure symptoms. Other risk models exist (CARPREG: CARDiac disease in PREGnancy and ZAHARA)^{12,13}; however, a recent publication found that the WHO classification had greatest accuracy in predicting maternal outcomes. No model predicted fetal events with sufficient accuracy as to be of utility.¹⁴

Exercise testing may be useful, although there are little data^{15,16} for risk stratification. Our centres (Royal Melbourne Hospital (RMH) and Royal Prince Alfred Hospital (RPAH)) undertake assessment with a pre-conception stress test with oximetry (exercise or cardiopulmonary stress test), clinical review, electrocardiography (ECG) and echocardiography. Cardiac MRI may also be useful, particularly if there are concerns about thrombus or possible obstruction in the Fontan pathway, to ascertain the presence of collaterals and for quantification of ventricular function, especially if echocardiographic imaging is of limited quality.¹⁷

Importantly, pre-conception review may allow identification and management of potentially reversible complications (e.g. radiofrequency arrhythmia ablation or shunt closure). Guidelines suggest counselling against pregnancy in the presence of oxygen saturation less than 85%, reduced ventricular function, moderate or greater atrio-ventricular regurgitation or protein-losing enteropathy.¹¹ Clinical concerns of Fontan failure, with contemplation of Fontan revision or heart transplantation, are absolute contraindications to pregnancy.

Despite being well informed of the potential risks, women may still choose to pursue pregnancy due to the strong desire to become a parent. Drenthen et al.¹⁸ reported that a proportion of women with Fontan circulation counselled against pregnancy were still 'contemplating' pregnancy. We have shown that the spread of medical advice given regarding pregnancy was no different between women who did and did not report a pregnancy.¹⁹ It is also possible that this reflects medical limitation in risk stratification.

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Contraceptive use

The choice of contraception results from physician advice and patient preference. Guidelines recommend progesterone-only pills or dermal implants. The levonorgestrel-releasing intra-uterine device is described as second line, with recommendation of insertion in hospital due to the risk of a vasovagal reaction.¹¹ Estrogen-containing contraception (COCP) is contraindicated,²⁰ due to thromboembolic (TE) risk.²¹ Nonetheless, a significant proportion of surveyed women with a Fontan circulation report COCP use.¹⁹ This likely highlights the need to balance COCP risk with pregnancy risk. Clinical compromise of risk mitigation with anticoagulation may underpin this decision making in some women. The use of COCP should be consulted with the cardiologist.

Fertility concerns

Publications report significant subfertility in women with a Fontan circulation (18–21%),^{19,22} compared to approximately 9% in the general population.²³ Chronic disease^{24–27} and clotting abnormalities^{28,29} are possible putative contributors. Additionally, cyanosis has been described to affect fertility³⁰ and appears a plausible culprit; however, source data demonstrating causality were difficult to establish.

Miscarriage

Miscarriage appears more common, estimated at 42%²⁰ in our local data, greater than the ‘usual’ 20% reported in the general population.³¹ It is possible that an impaired capacity to increase cardiac output, elevated systemic venous pressure, abnormal platelet and endothelial cell activation³² and cyanosis all uniquely affect the process of implantation and uterine angiogenesis.

Maternal considerations during pregnancy

Physiology and pathophysiology

Pregnancy has a number of cardiovascular physiological effects. There are hormonally mediated changes in heart rate and intravascular volume,^{33–37} changes in the autonomic nervous system³⁸ with a proarrhythmic effect,³⁹ and, in healthy women, an asymptomatic reduction in cardiac systolic⁹ and diastolic function at term.^{9,40} Pregnancy and the puerperium are hypercoagulable states.³⁴ These physiological effects of pregnancy may combine to increase complications in women with a Fontan operation, who are already at risk of developing atrial arrhythmias,^{21,41,42} ventricular dysfunction^{1,43} and TE events (particularly in the older style atriopulmonary Fontan connection).^{21,44} Hypervolaemia and hypovolaemia may also pose significant challenges.^{45,46}

Cardiac symptoms in pregnancy

Managing any woman with cardiac disease in pregnancy can be challenging, with normal pregnancy causing symptoms and signs also seen in cardiac decompensation, e.g. palpitations, shortness of breath and ankle swelling.^{47–49} In the Fontan population, these merit cardiology assessment and may reflect atrial arrhythmias, cardiac functional decompensation or a poor chronotropic response, with an inadequate heart rate for the increased cardiac output requirement. Peripheral oedema may reflect an obstetric medical complication (pre-eclampsia, renal failure) but additionally may highlight an inability to cope with the increased cardiac demands and intravascular volume.

In these situations, it is invaluable to have pre-pregnancy cardiac test results to compare to with clinical review by the usual cardiology

team. Investigation with a Holter monitor, six-minute walk test with oximetry and echocardiography should be initiated at low thresholds of concern.

Medications in pregnancy

There is no consensus in the current congenital guidelines with regard to routine anticoagulation in the general Fontan population.^{11,20,50} Many centres have routinely anticoagulated the atriopulmonary (AP) patients; however, younger patients with a lateral tunnel (LT) or extra-cardiac connection (ECC), without atrial arrhythmias or a large right to left shunt, are often on aspirin.

In pregnancy, guidelines^{11,20} state that anticoagulation should be considered in this population. It seems difficult to cease anticoagulation in a woman anticoagulated prior to pregnancy, given the pregnancy related increase in both TE events and atrial arrhythmias, in the general population. The most recent American guidelines on complex congenital heart disease and pregnancy state that in women with pre-pregnancy anticoagulation, the need to continue during pregnancy is controversial but would seem to be justified if there is a prior TE event or atrial arrhythmias.⁵¹ Anticoagulation needs to be discussed with every woman, ideally pre-conception.¹¹

Emerging literature suggests that antepartum and postpartum bleeding may be more common in these women,⁵² adding to the difficulties in anticoagulation decision making for both mother and fetus. A current multi-institutional retrospective study (PROFAT: PRenancy Outcomes in Fontan's with Anticoagulation Therapy) aims to evaluate bleeding and thrombotic complications and will add to knowledge.⁵³

In general terms, available options are low-molecular weight heparin (LMWH), either at a prophylactic (deep vein thrombosis (DVT) prevention) or therapeutic dose or warfarin. Most of the data on use of these agents in pregnancy are derived from other cardiac medical conditions. Warfarin is associated with increased rates of miscarriage, embryopathy and central nervous system (CNS) abnormalities in the infant.⁵¹ Embryopathy is more common at dosages >5 mg/d and with exposure between 6 and 9 weeks' gestation.⁵¹ These factors may make LMWH more appealing, and, at a minimum, if anticoagulation is decided upon, LMWH should be used in the first trimester. LMWH needs to be weight adjusted. Antifactor Xa levels do not require the frequent (weekly) monitoring recommended for mechanical valves,¹¹ but it would seem prudent to have clinical oversight by a haematologist with regular monthly antifactor Xa levels, particularly in view of the increased bleeding risk. LMWH may cause thrombocytopenia, osteoporosis and allergic skin reactions. Timing of doses needs to be considered, both for checking antifactor Xa levels and neuraxial anaesthesia.⁵⁴

Fontan patients are more likely to be prescribed anti-arrhythmics, angiotensin-converting enzyme inhibitors (ACEI) and diuretics than other CHD patients.⁵⁵ The data on ACEI use in the Fontan population remain largely anecdotal with a recent ANZ Fontan Registry data showing 36% of patients are prescribed an ACEI,⁵⁶ despite little evidence of benefit. ACEI are implicated in fetal renal damage^{57,58} and should ideally be ceased pre-conception or at the first confirmation of pregnancy.⁵⁹ The commonest reason for beta blockade prescription in this group is to treat maternal atrial arrhythmias, which can adversely affect maternal health and require repeated cardioversion. Nonetheless, the use needs to be accompanied by consideration and discussion of risks as oral beta-blockers have been associated with fetal growth restriction,⁶⁰ low birthweight, increased risk of delivering small for gestational age (SGA) infants⁶¹ and neonatal bradycardia and hypoglycaemia.⁶² Diuretics decrease placental blood flow⁶³ and should be used at the lowest effective dose.¹¹ Spironolactone causes electrolyte disturbances and endocrine dysfunction in fetuses of both genders, including feminisation of the male fetus and is contraindicated in pregnancy. The use of cardiovascular medicines in pregnancy is well covered in a recent review.⁶⁴

Maternal outcomes in the literature

In the short-term, pregnancy in the Fontan circulation has been shown to increase maternal morbidity. In published series (excluding single case studies and not limited to live births if the data set was reported regardless of fetal outcome), described outcome ranges are atrial arrhythmias (5–21%),^{19,22,65,66} pregnancy-related bleeding (5–50%)^{19,22,65,66} and heart failure (7%).^{19,22,65} Cases of NYHA deterioration,^{12,18,22,66} TE events^{22,66} and hypoxemia^{22,66} have also been reported.

Despite the above, published series describe women without significant morbidity and some who have undergone multiple pregnancies. Published series have not reported maternal deaths.^{19,22,65–68} A publication by Canobbio et al.⁶⁹ describes five late deaths (TE (n = 2), ventricular failure (n = 2) and unknown (n = 1)), in 45 women reporting 71 pregnancies, raising a question about longer term sequelae. Late effects of pregnancy have been suggested in other conditions,^{6,7,70} and this should be raised, at least as a theoretical risk, in pre-conception counselling.

Fetal concerns in pregnancy

The risk of premature delivery, fetal mortality and SGA offspring is greater in women with a Fontan circulation.^{19,22,67}

Publications report significant rates of preterm delivery, ranging from 39% to 81%.^{18,19,22,65,66} It is difficult to account for possible iatrogenic contribution, with medical decision making for earlier delivery influenced by concerns about maternal well-being and/or poor fetal growth.

Excess frequency of preterm premature rupture of membranes (PPROM) in the Fontan subgroup has been reported⁷¹ and PPRM should be managed as per accepted guidelines.^{72,73} PPRM may carry a greater fetal risk in this population, as the fetus may be smaller than anticipated by gestational assessment.

A retrospective series of CHD mothers described SGA as affecting 25% of neonates but was higher (38%) in the subgroup with maternal cyanosis.⁷⁴ SGA offspring in women with CHD in general has been attributed to placental insufficiency⁷¹ and abnormal hemodynamics,⁷⁵ although there is little published information on this. Routine ultrasound scanning to assess placental function may assist timing of delivery by identifying fetuses at increased risk.⁷⁶

Fetal and neonatal deaths are always highly distressing for all involved, and both have been reported in this population: in maternally uncomplicated pregnancies¹⁹ as well as in women with PPRM and placental abruption.²² Neonatal deaths reported appear related to complications of prematurity.^{18,19,22} It is likely that neonatal survival depends more on access to specialised neonatal intensive/special care services and is largely dictated by gestational age and weight, rather than maternal cardiac disease, post-delivery.

Cardiac disease in the offspring

The genetic contribution to CHD remains poorly understood. However, familial clustering and affected offspring are uncommon. This suggests that most CHD is the end-product of a multifactorial process, without a single major genetic contribution. Overall, in the absence of an autosomal dominant condition (e.g. 22q11 deletion), women with CHD are estimated to have a 3–8% risk of having a baby with CHD¹² compared with a background population rate of 1% of live births.⁷⁷

Care during pregnancy

Antenatal care

Antenatal care should commence pre-conception, and the team expand as required during pregnancy to involve cardiologists, obstetricians,

anaesthetists (obstetric and cardiac), haematologists, neonatologists and intensive care physicians. Experienced midwifery and nursing staff as well as allied health professionals should also be actively involved.

Confirmation of pregnancy should lead to re-checking of all medications and immediate contact with the treating haematologist, for institution of an anticoagulation plan if required.

As discussed earlier, no CHD guideline offers unequivocal advice regarding anticoagulation management during pregnancy.^{11,51}

Frequent cardiology review (at least each trimester and with increasing frequency as pregnancy progresses) with echocardiography and measurement of oxygen saturation is important, to ascertain the emergence of cardiac symptomatology and assess the presence of fluid overload and ventricular function. Additionally, individuals with a Fontan circulation and reduced oxygen saturation should have a compensatory erythrocytosis and thus increased hematocrit requirements. This will be of greater importance in pregnancy, which is often accompanied by anaemia and iron deficiency.⁷⁸ A woman may have a haemoglobin level that falls within the 'normal range' but have important iron deficiency and thus iron levels should be checked regularly and replaced as required.⁷⁹ The limited capacity to increase cardiac output⁴⁵ may contribute to reduced maternal functional status and women should be medically supported in ceasing/reducing employment and aiming for a daily rest, if symptoms of fatigue emerge.

Management of birth

Planning for birth involves maternal and fetal considerations, assessment of the risks and benefits of vaginal versus caesarean birth, and the capabilities of the specialised centre to deliver emergency cardiac, obstetric, anaesthetic and neonatal care. Multidisciplinary consideration of possible scenarios, from planned elective caesarean section (CS) to emergency birth after hours, and contingency planning for cardiac decompensation and obstetric haemorrhage should occur.

Planned vaginal birth, with scheduled in-hours induction, has the advantages of reduced blood loss, smaller blood volume shifts and fewer clotting complications.^{11,52,80} Haemodynamic monitoring during labour includes ECG, pulse oximetry and blood pressure monitoring, which may include an intra-arterial pressure monitor.

In the absence of contraindications, a slowly titrated early lumbar epidural provides excellent analgesia and haemodynamic stability. It also allows an instrumented second stage, minimising the haemodynamic stress of the Valsalva manoeuvre. Experienced midwifery and critical care trained staff are essential.

The disadvantages of vaginal birth include the unpredictability of the progress of labour, the possibility of an emergency or immediate CS being required, reduced likelihood of success if preterm, and the possibility of a birth occurring after hours when staff numbers are often reduced. If the mother is anticoagulated, there is concern about fetal intracranial bleeding. Transition to intravenous heparin or planned induction with cessation of LMWH the day before may then be considered.

In the case of planned CS, slow, incremental dosing of epidural for CS is recommended^{81,82} to reduce the risk of decreased preload; this is important as preload drives circulation in the Fontan circuit.^{45,82}

While the number of cases published are small, emergency CS rates following onset of labour appear higher,⁸¹ compared to the general population (0.5–1%).⁸³ In such cases, general anaesthesia may be deemed necessary. This should be undertaken cautiously in this population, as positive pressure ventilation may adversely affect hemodynamic status.⁸¹

Postpartum

The postpartum period also carries risk. Postpartum haemorrhage, with an increased need for blood transfusions or return to theatre

appears to occur more commonly in this population.^{18,19,52} The auto-transfusion phenomena, with uterine blood entering the systemic circulation, may precipitate decompensation in the 48–72 h after delivery, increasing the risk of cardiac failure and pulmonary oedema. It is recommended that women with a Fontan circulation be monitored in a high acuity unit during this time. A desire to breastfeed should be supported, if possible.

Thromboprophylaxis needs to be agreed upon in discussion by the cardiologist and obstetrician, and anaesthetist if neuraxial anaesthesia has been utilised. At minimum, all women should have DVT prophylaxis post CS. Women with pre-pregnancy indication(s) for anticoagulation should be anticoagulated post delivery once deemed safe. Haemoglobin and iron levels should be optimised in the postpartum period and contraception should be prescribed by discharge.

Follow-up with a repeat echocardiogram and cardiology review at approximately 6–12 weeks' postpartum is recommended.

Subsequent pregnancies

It is important to recognise that having one successful pregnancy does not guarantee a subsequent successful outcome. Thus, women should be re-assessed prior to any future planned pregnancies. Anecdotally, our experience has been that women feel a greater responsibility for the child they have than the one they might have and are often less willing to accept an adverse pregnancy risk assessment after their first pregnancy.

Life expectancy

Life expectancy remains unknown in this population, reflecting the limited time since operation inception, and the anticipation that newer iterations of the Fontan operation may improve long-term outcomes. Current long-term follow-up data report long term survival at 75%, 25 years after the original, AP Fontan procedure.⁴¹ However, there are concerns about the longevity of the Fontan circuit and the emergence of 'Fontan failure'.⁸⁴ It is important to be honest with patients about the unknowns, but also refrain from what is currently a judgement call regarding long-term maternal survival.

Therefore, balancing concerns about longer-term survival against a decision to have a child are to be made by the woman and her partner. Medical advice against conception should be reserved for women where pregnancy itself is assessed to carry a significant risk of death or heart failure.

Importantly, a recent publication showed survival benefit when cared by a cardiologist with training in congenital heart disease for the Fontan population,²¹ and it would appear reasonable to extrapolate that care continuum to pregnancy.

Conclusions

The numbers of Fontan women who have gone through pregnancy are small. Successful pregnancy is achievable, although there is an increased risk for maternal and fetal complications. Current data suggest that fetal morbidity is significantly higher than maternal morbidity. However, the long-term implications for maternal cardiac function are unknown. The importance of pre-conception counselling, risk individualisation and creation of an early management plan, particularly around cardiac medication cessation/alteration and anticoagulation, and planning for birth cannot be overemphasised.

Pregnancy should be managed in a specialised multidisciplinary environment with regular reviews involving a range of medical specialists, midwives and nurses. Additional care such as psychological support, particularly for women encountering pregnancy loss or a traumatic ill-health trajectory through pregnancy may also be required.

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DZ conceived the idea for the review. The literature search and appraisal, and drafting and editing of all article versions were undertaken by EM and DZ. All authors have contributed to, reviewed and approved the final version of the draft.

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