JACC Vol. 28, No. 3
September 1996:763–7

Pregnancy Outcomes After the Fontan Repair

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Objectives. **This study sought to determine risks and outcome of pregnancy and delivery after the modified Fontan operation.**

Background. **Increasingly, female Fontan patients reaching child-bearing years are interested in having children. To date, the number of reported pregnancies is small, and pregnancy has therefore been discouraged.**

Methods. **One hundred ten of 126 female patients from the Fontan registries of the Mayo Clinic and University of California Los Angeles Medical Center responded to a mailed questionnaire. An additional six patients with a reported pregnancy from other centers were identified and reviewed to assess pregnancy outcomes.**

Results. **Among the participating centers, a total of 33 pregnancies after Fontan operation for various types of univentricular heart disease were reported. There were 15 (45%) live births from 14 mothers, with 13 spontaneous abortions and 5 elective terminations. In the 14 women with live births, the median number of years between operation and pregnancy was 4 (range 2 to 14). Reported prepregnancy problems in these gravidas included atrial flutter in one patient and ventricular dysfunction, aortic regurgitation and atrioventricular valve regurgitation in another. One patient developed supraventricular tachycardia during pregnancy and had conversion to sinus rhythm. No maternal cardiac complications were reported during labor, delivery or the immediate puerperium. There were six female and nine male infants (mean gestational age 36.5 weeks; median weight 2,344 g). One infant had an atrial septal defect. At follow-up, mothers and infants were alive and well.**

Conclusions. **Pregnancy after the Fontan operation appears to have been well tolerated in 13 of 14 gravidas. There does appear to be an increased risk of miscarriage. The tendency to routinely discourage pregnancy may need to be reconsidered.**

(J Am Coll Cardiol 1996;28:763–7)

The Fontan and now the modified Fontan procedures have become recognized as the most definitive operation available for a number of complex congenital heart defects characterized by a functional single ventricle. Increasing numbers of postoperative women are now reaching their childbearing years, and many desire to have children. However, to date, the number of reported pregnancies and live births in this population has been small (1–7). Because of the unlikelihood of any one center having numerous pregnancies, it has been difficult to determine the true risk of pregnancy and delivery to the post-Fontan patient and her infant. A multicenter study was therefore undertaken to determine the pregnancy outcomes after modified Fontan operation and to determine the risk of pregnancy and delivery to the post-Fontan female patient and her infant.

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Manuscript received February 16, 1995; revised manuscript received April 17, 1996, accepted May 3, 1996.

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Methods

Patients. The study cohort was drawn in part from the Fontan registries of the Mayo Clinic and the University of California Los Angeles (UCLA) Medical Center. Post-Fontan female patients who had reached menarche were asked to respond to a mailed questionnaire designed to determine pregnancy and contraceptive experiences after modified Fontan repair. Of the 126 eligible female patients, 110 responded, with 16 nonresponders who were lost to follow-up. Additionally, six centers (see Appendix) with Fontan pregnancies were invited to participate. For subjects who reported a live birth, the medical records and, where possible, the obstetric records were reviewed.

Results

This collaborative effort identified 21 of 118 subjects as having a total of 33 pregnancies after the Fontan procedure. Fifteen (45%, 95% confidence interval [CI] 28% to 60%) pregnancies resulted in live births, 5 (15%, 95% CI 6% to 29%) in elected therapeutic abortions for noncardiac reasons and 13 (39%, 95% CI 23% to 54%) in spontaneous abortions during the first trimester. One woman was taking the fertility drug clomiphene citrate and had three spontaneous miscarriages. If this patient is removed from the series, the first-trimester miscarriage rate was 33% (95% CI 18% to 49%).

0735-1097/96/$15.00
PII S0735-1097(96)00234-3

Table 1. Diagnosis and Surgical History of 14 Post-Fontan Mothers

Pt No.	Defect	Type of Connection	Age at Operation (yr)	Postoperative Complications Before Pregnancy	Postoperative Medications During Pregnancy
1	T. atresia	Atriopulmonary anastomosis	22	Atrial flutter	Digoxin, quinidine
2	T. atresia	Atriopulmonary anastomosis	14	None	Digoxin
3	T. atresia	Atriopulmonary anastomosis	15	None	None
4	T. atresia	RA-RV Hancock conduit	24	None	None
5	DILV	#1 RA-RV Hancock conduit	23		
		#2 Atriopulmonary anastomosis	32	None	None
6	T. atresia	Atriopulmonary anastomosis	26	None	None
7	T. atresia	RA-RV Hancock conduit	14	None	None
8	DILV	Atrial pulmonary Hancock conduit	11	None	None
9	T. atresia	#1 RA-RV Hancock conduit	5		
		#2 RA-RV Carpentier conduit	10	None	None
10	DORV/hypoplastic RV	Cavopulmonary anastomosis	22	None	None
11	TGA/straddling TV/hypoplastic RV	#1 Atriopulmonary anastomosis	14		
		#2 Redo patch closure RAVV	15	None	None
12	DORV/hypoplastic RV	Cavopulmonary anastomosis	21	AVVI, LV dysfunction	Quinidine
13	DORV/hypoplastic RV, polysplenia	Cavopulmonary anastomosis	18	Periodic SVT	Digoxin
14	UVH of LV type with right AVV atresia	Atriopulmonary anastomosis	17	Atrial flutter with 1:1 conduction; ventricular rate 265 beats/min	Tenormin/digoxin

AI = aortic valve insufficiency; AVVI = atrioventricular valve insufficiency; DIRV = double-inlet left ventricle; DORV = double-outlet right ventricle; LV = left ventricle; Pt = patient; RA-RV = right atrial to right ventricle; RAVV = right atrioventricular valve patch closure; RV = right ventricle; SVT = supraventricular tachycardia; T = tricuspid; TGA = transposition of the great arteries; TV = tricuspid valve; UVH = univentricular heart.

Fourteen gravidas carried their pregnancies to a live birth, with 1 having two successful pregnancy outcomes. These 14 women and their 15 children form the study cohort for the present report.

Cardiac anomaly and surgical history. The median age at Fontan operation of patients subsequently becoming pregnant was 17 years (range 10 to 32). Diagnoses and surgical history of the patients are summarized in Table 1. Two patients (Patients 5 and 9) required reoperation after their original Fontan procedure. Postoperative complications also are listed in Table 1. Atrial arrhythmias after the Fontan operation were reported in four patients. One patient (Patient 1) developed atrial flutter that required treatment initially with digoxin (0.125 mg twice daily) followed by cardioversion and then quinidine (300 mg three times daily) (2). At the time of her pregnancy she was in sinus rhythm. Patient 12 was given quinidine preoperatively and postoperatively for supraventricular and ventricular tachycardia. Patient 13 had periodic supraventricular tachycardia that has been controlled with digoxin; Patient 14 was treated for atrial flutter with intermittent 1:1 conduction and a ventricular rate of 265 beats/min. The remaining patients were reported to be free of significant heart rate abnormalities. Apart from arrhythmias, the only other reported post-Fontan cardiac problem involved Patient 12. At the time of her pregnancy she was known to have mild aortic regurgitation, atrioventricular (AV) valve regurgitation and some degree of ventricular dysfunction.

Pregnancy history. At the time of pregnancy the 14 study subjects ranged in age from 18 to 36 years (median age 24). These 14 patients had 25 of the total 33 pregnancies. Pregnancy, for the 15 live births, occurred at a median of 4 years (range 2 to 13) after the Fontan procedure.

The median gestational age of the newborns was 38 weeks (range 28 to 40). Footling breech presentation, failure to progress and preterm labor at 28 weeks were the obstetric indications for 3 of the 11 cesarean sections. For the remaining eight, the reason for cesarean delivery was unclear from review of the obstetric records. Epidural anesthesia was used for 10 deliveries, spinal for 2 and general anesthesia for 1. One woman delivered by natural childbirth. The anesthesia method for the remaining delivery is unknown.

Cardiac complications. For 12 of the 14 mothers, there were no significant cardiac complications reported throughout the antepartum, labor, delivery or postpartum period. Patient 7 developed supraventricular tachycardia in her 27th gestational week, requiring hospital admission. She was started on digoxin (0.25 mg/day) and verapamil (80 mg/day) therapy. At 38.5 weeks, she developed recurrent supraventricular tachycardia with a heart rate of 180 beats/min and complained of weakness and breathlessness. She had conversion to sinus rhythm with 5 mg of intravenous verapamil. Patient 12 reportedly complained of mild shortness of breath throughout her pregnancy and immediately after delivery. She was treated with oxygen for 1 week and discharged. Subsequently, she was treated for congestive heart failure with afterload-reducing agents. There were no other reported cardiac complications during the postpartum period. No cardiac medications were initiated during any of the other pregnancies. However in Patient 1, the quinidine dose was increased from three to four times per day during the pregnancy. Two patients complained

of periodic palpitations during the pregnancy, but no treatment was necessary.

Noncardiac complications. Peripheral edema occurred in two patients. Patient 6 had spontaneous premature rupture of the membranes at 34 weeks and later developed an incarcerated left inguinal hernia involving the left ovary, necessitating a herniorrhaphy. The patient recovered without further consequences.

Maternal outcomes. At 18 months after delivery, no adverse clinical sequelae were evident for 13 of the 14 women. Patient 12 has continued to be treated for ventricular failure, but at 20 months, her cardiovascular function has returned to prepregnancy status.

Infant outcomes. There were six female and nine male infants. Birth weight ranged from 1,050 to 3,575 g (median 2,344). Only one child was born prematurely at 28 weeks' gestation and weighed 1,050 g. At 4 years old, the boy has developed normally. One infant had a congenital anomaly, an atrial septal defect that has since been surgically closed. All infants are currently alive and well.

Prepregnancy counseling. Because physicians tend to advise the female Fontan patient against pregnancy, included in the UCLA/Mayo Clinic questionnaire were questions that addressed pregnancy counseling. Of the 76 patients who responded to this question, 50 (66%, 95% CI 54% to 75%) indicated that they had been advised by a physician not to become pregnant despite a clinically stable surgical outcome and a strong desire to have children. The remaining 26 patients (34%, 95% CI 23% to 44%) indicated they had not been advised about pregnancy. With respect to contraception, there were 83 responses. Thirty-two indicated that they used no form of contraception; 21 said that they used some form of barrier method; and 14 used oral contraception. Fourteen had undergone tubal ligation (seven before and seven after their Fontan procedure), and two had a hysterectomy after their Fontan procedure.

Discussion

The goals of the original Fontan procedure (8) and its subsequent modifications have been to eliminate intermixing of pulmonary and systemic venous return, thereby achieving a normal oxygen tension in the systemic arterial circulation, and normalizing the volume load on the functional single ventricle. These goals can be accomplished only at the price of elevated systemic venous and right atrial pressures. In the absence of a ventricle pumping to the lungs, a minimal pressure of 12 to 14 mm Hg is necessary in the right atrium and systemic veins to achieve an adequate driving pressure across the pulmonary capillary bed (9). Fontan patients with a mean right atrial pressure ≥20 mm Hg immediately after repair have been reported to have an increased surgical mortality and late morbidity (9,10). Late postoperative complications associated with the Fontan procedure include arrhythmias, protein-losing enteropathy and thromboembolic events, with atrial arrhythmias the most frequently cited (11). Probably due to persistent elevated right atrial pressure and increased wall tension, the most prominent arrhythmias have been supraventricular tachycardia and atrial flutter or fibrillation. In most series, including ours, arrhythmias have been well controlled with standard medical therapy.

In women with congenital heart disease, pregnancy outcomes have been shown (12) to be related to functional cardiac status, anatomic diagnosis, pulmonary vascular resistance, type of operation and degree of residual impairment. In women with cyanotic heart disease, maternal mortality ranges between 4% and 16% in uncorrected lesions (13). Tetralogy of Fallot, the only cyanotic lesion for which postoperative pregnancy data are widely available, carries a postrepair pregnancy risk similar to that of the general population (14,15). Little pregnancy data are available for other corrected cyanotic lesions.

For post-Fontan patients, questions have focused on the ability of the right atrium and functioning single ventricle to generate and tolerate the normal cardiovascular adjustment to pregnancy, including increases in cardiac output (30% to 40% above nonpregnant levels), circulating volume (up to 50%) and heart rate that normally occur during pregnancy. Because the post-Fontan patient has limited ability to increase cardiac output despite an elevated venous pressure, concern has been raised about her ability to cope with the increased physiologic demands of pregnancy and delivery. The present study and others report a total of 22 term pregnancies. Among these, there have been no reported maternal deaths or serious morbidity. There have been two reported neonatal deaths due to prematurity (4,5). In both cases the mothers developed arrhythmias during pregnancy. In one case the mother had persistent junctional tachycardia (4), and in the other the mother developed atrial flutter with 2:1 AV block (5). The current series has the only reported case of congenital heart disease in the offspring.

Although the number of cases is still small, it appears that the post-Fontan patient who is clinically well before pregnancy is able to tolerate the additional hemodynamic burden of a term pregnancy and delivery and to return to her prepregnancy level of function once her convalescence is complete. However, this same experience suggests that the incidence of first-trimester spontaneous abortion in post-Fontan patients (33%) appears to be twice that in the general population (15%) (16).

Still unknown is whether pregnancy will have any long-term residual effect on a myocardium previously exposed to years of hypoxia and volume overload. With Fontan surgery being performed at younger ages, these effects on the functional single ventricle may be less important in the future.

For the infant, the risk of congenital heart disease remains unknown. In the present series, the incidence rate was 6%, which is within the 3% to 8% range often quoted for infants born to women with congenital heart disease (17,18). Advances in fetal echocardiography, including transvaginal echocardiography, should eventually permit identification of most major fetal anomalies during the first trimester (19).

This clinical experience suggests that women who are in clinically stable condition after the Fontan operation will

tolerate pregnancy and delivery. A woman who is doing well and desires to have a child should not be routinely discouraged from doing so. Rather, she should be made aware of the potential risk to her and her child, including the possible increased incidence of first-trimester miscarriage. To provide the mother with accurate information about the risk that a pregnancy may pose, a comprehensive evaluation, including electrocardiography and Doppler echocardiography to evaluate ventricular function and AV valve competency and to check patency of the right-sided Fontan pathway, should be performed before pregnancy. If potential concerns are identified by Doppler echocardiography, a short cardiac catheterization to provide more precise information, including cardiac output and right-sided pressures, may be indicated.

Contraception. Prepregnancy counseling should be an integral part of routine cardiac follow-up care. Patients should be advised of the importance of planning a pregnancy and counseled about appropriate forms of contraception. In the UCLA/Mayo study, 38% (95% CI 27% to 49%) of the respondents reported using no form of birth control, whereas an additional 14% (95% CI 7% to 23%) used oral contraception. Because of the increased potential for intracardiac thrombus formation, estrogen-based contraception is contraindicated (20). Although the risk of infective endocarditis in post-Fontan patients is low, use of intrauterine devices may still be ill-advised. Combined barrier methods (i.e., diaphragm with spermicide), controlled-release progestin (Norplant) or Depo-Provera are probably the safest contraceptives for these patients (21).

Management. A pregnant post-Fontan patient requires collaborative management, including a cardiologist, a high risk obstetrician and anesthesiologist familiar with adult congenital heart disease and the cardiovascular changes of pregnancy and parturition. Ideally, the gravida should be followed up at a specialized center that has experience both with post-Fontan patients and high risk pregnancy. Peripheral edema, breathlessness and fatigue are common findings in normal pregnancy and do not necessarily indicate cardiac decompensation (22). Because of their limited cardiac reserve, it would be prudent for these patients to avoid strenuous exercise (such as heavy lifting), to take daily rest periods and to limit their salt intake.

Observed maternal cardiovascular changes occurring during labor and delivery pose additional risk. For example, during the first stage of labor, cardiac output normally increases by ~25% between uterine contractions, with further elevations during contractions. However, because of compression of the inferior vena cava by the gravid uterus, the supine position at term gestation decreases stroke volume and cardiac output by ~25% and may result in maternal bradycardia and hypotension (23). To minimize these effects, it is important to have the gravida labor in a lateral position. Epidural anesthesia is recommended because it promotes hemodynamic stability by reducing pain-related increases in sympathetic activity. However, epidural anesthesia should be used cautiously, or not at all, if cardiac output is suspected to be unusually sensitive to decreases in preload. In such high risk patients, narcotic epidural and continuous narcotic spinal anesthesia are a good alternative during labor, with general anesthesia reserved for cesarean delivery. A vaginal delivery should be expected with an assisted second stage of labor so as to avoid the reduction of venous return caused maternal Valsalva maneuvers. Cesarean delivery is reserved for obstetric indications (23,24). Immediately after delivery, patients should be closely monitored because cardiac output in normal women increases by as much as 75% over predelivery values (25). This increase is of particular concern in women who may not tolerate volume shifts or who are unable to increase their cardiac output in response to increased demand (26). Therefore, volume shifts should be monitored carefully and the mother left on her left side during the immediate postpartum period. The effect may persist for ~1 week but returns toward normal within 2 weeks (23–25).

Study limitations. To our knowledge, this is the largest clinical series reported on pregnancy outcomes in post-Fontan patients; however, certain limitations need to be considered. Patient selection was a sample of convenience and is representative, therefore, only of post-Fontan patients followed up principally at a few centers; there are undoubtedly other patients who have become pregnant and have not been identified by this relatively informal sampling. In turn, if some of these patients had developed complications, the overall outlook is less favorable. Another potential bias is that for logistic reasons, obstetric care data were obtained through correspondence and often relied on the memory of the obstetrician or cardiologist rather than direct inspection of the medical record.

Another limitation is that little is known of patients' hemodynamic status after the Fontan procedure and before pregnancy; data were not consistently available, in part because several pregnancies were not planned, and in part because hemodynamic studies are not part of routine follow-up care. Optimally, however, a clinical and hemodynamic baseline of functional status would be established before conception. Finally, the numbers of patients in the present study are too few to predict safety; however, with one exception all patients were in functionally stable condition before pregnancy.

Conclusions. The number of female post-Fontan patients reaching adulthood and desiring to have children will continue to increase. These women are limited in their ability to increase cardiac output in response to exertion or the increased physiologic demands of pregnancy and have generally been counseled by their physicians to avoid pregnancy. A larger patient series and longer follow-up periods are clearly needed before the risk of pregnancy and delivery to these patients and their infants can be precisely defined; based on our experiences with 14 patients, however, it seems unreasonable to prohibit pregnancy in the patient who has a good postoperative result. Such patients should be made aware of the clinical experiences to date and the potential risks to them and their fetus, including the possibility of a reported increased risk for first-trimester abortion, which will help them to make an informed decision regarding pregnancy.

Appendix

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