Pregnancy Outcomes After Atrial Repair for Transposition of the Great Arteries

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Increasingly, women born with complete transposition of the great arteries who have undergone atrial repair by either the Senning or the Mustard procedure are reaching childbearing age. This study reports on pregnancy outcomes after the atrial repair of transposition of the great arteries. Record review and standardized questionnaires were used to ascertain the outcomes of 70 pregnancies reported in 40 women (36 Mustard procedures, 4 Senning procedures). Of the 70 pregnancies, 54 resulted in 56 live births, 10 in miscarriages, and 6 in therapeutic abortions. At pregnancy, 31 women were in New York Heart Association class I, 8 were in class II, and 1 was in class III. Thirty-nine percent of the infants were delivered prematurely and weighed 2,714 ± 709 g; 28% were delivered by cesarean section, 8 for cardiac indications. Maternal complications included arrhythmias in 5 women and hemoptysis in 2 women. Heart failure occurred in 6 women, developing during the second and third trimesters. Postpartum cardiac events developed 2 to 9 days postpartum: heart failure in 5 women, atrial fibrillation in 1 woman, and decreased oxygen saturation due to a new atrial baffle leak in 1 woman. Severe right ventricular (RV) failure led to cardiac transplantation after delivery in 1 woman; another developed heart failure and then died suddenly 1 month after delivery. There was 1 late death, 4 years after the patient's last pregnancy. In conclusion, pregnancy after atrial repair carries a moderate degree of risk and should be undertaken with caution. **(Am J Cardiol 2006;98:668–672)**

Because of the limited experience that any single center may have in pregnancy outcomes in women with complex congenital heart defects, a national registry of women who became pregnant after surgical repair for complex congenital heart defects was organized in 1996. Herein, we report the initial findings on pregnancy after atrial repair for transposition of the great arteries (TGA) to determine the prevalence of adverse maternal and infant outcomes in women after Mustard and Senning repair and to determine maternal factors associated with adverse outcomes.

Methods

A public announcement was placed in publications of the American Heart Association and the International Society of Adult Congenital Cardiac Disease. The entry criteria were having undergone atrial correction for TGA and having experienced a pregnancy after surgical repair. Practitioners wishing to enroll a subject to this collaborative registry contacted the registry office and were sent standardized forms for data collection. After institutional review board approval, data were retrospectively abstracted from the obstetric records for pregnancy, delivery, fetal outcomes including cardiac and obstetric complications during pregnancy, mode of delivery, anesthesia, medication use, and length of stay for delivery. Medical, diagnostic, and surgical data also were requested, including pre- and postpregnancy cardiac morbidity, arrhythmias, medications, echocardiographic results, and postpartum cardiac follow-up. Information on 76 pregnancies in 40 women from 16 centers was received, but 7 additional pregnancies from 1 center were not included in this analysis because of incomplete data.

Because of multiple pregnancies within the cohort and changing medical status before pregnancy, each pregnancy was considered an independent event. In the event of multiple births (twins), the pregnancy was counted once, but each fetal outcome was recorded. Means and SDs were computed for these data as appropriate. Proportions were compared using a chi-square distribution, and means were tested by Student's *t* test.

Results

A total of 70 pregnancies were contributed from 40 women from 16 centers (see the Appendix) in the United States. These pregnancies occurred from 1985 to 2002. The prepregnancy medical status of these patients is listed in

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Table 1
Maternal cardiac status before pregnancy in 40 women with atrial switch surgery for dextro–transposition of the great arteries

Variable	Value
Age at definitive repair (mo) (range)	34.1 ± 37.3 (4–180)
Type of repair	
Mustard	36 (90%)
Senning	4 (10%)
Other heart defects	
VSD	1 (2%)
Pulmonic stenosis	3 (8%)
VSD and pulmonic stenosis	5 (12%)
Reoperation before pregnancy	6 (15%)
AV block before pregnancy	12 (30%)
First degree	6 (15%)
Third degree	5 (12%)
Unknown	1 (2%)
Arrhythmia before pregnancy	16 (40%)
Atrial flutter	5 (12%)
Supraventricular tachycardia	5 (12%)
Junctional rhythm	3 (8%)
Atrial fibrillation and flutter	1 (2%)
Nonsustained ventricular tachycardia	1 (2%)
Atrial and ventricular ectopy	1 (2%)
Pacemaker	13 (32%)
Functional class before pregnancy	
I	31 (78%)
II	8 (20%)
III	1 (2%)
Cardiac medications before pregnancy	
None	29 (72%)
Digitalis	10 (25%)
Atenolol	3 (8%)
Norpace	1 (2%)
RV function before pregnancy	
Normal	16 (40%)
Decreased	18 (45%)
Severely decreased	1 (2%)
Unknown	5 (12%)
Tricuspid regurgitation before pregnancy	
Normal or trace	9 (22%)
Mild to moderate	21 (55%)
Severe	1 (2%)
Unknown	8 (20%)

AV = atrioventricular; VSD = ventricular septal defect.

Table 1. All women had dextro-TGAs, and all but 4 women underwent Mustard repair (90%); the remainder underwent Senning repair. The atrial switch procedure was performed in childhood, at slightly <3 years of age on average (range 4 to 180 months, median 18). Nine women (22%) had associated cardiac defects: 5 with pulmonary stenoses and ventricular septal defects, 3 with pulmonary stenoses, and 1 with a ventricular septal defect. After definitive atrial switch repair, 6 women underwent reoperations for baffle leaks or pulmonary venous obstructions.

Atrioventricular blocks were noted in 30% of women, and 40% had arrhythmias before becoming pregnant. Atrial flutter and supraventricular tachycardia were the most common, followed by junctional rhythm and single cases of atrial fibrillation and flutter, atrial and ventricular ectopy, and nonsustained ventricular tachycardia. Thirteen women (32%) had pacemakers implanted for sinus node dysfunction or heart blocks. Immediately before pregnancy, 78% of women were in New York Heart Association functional class I, 20% were in class II, and 2% were in class III. Most women (72%) were receiving no cardiac medications at the time of pregnancy.

Table 2
Pregnancy outcomes and complications

Variable	Value
Outcomes	
Live birth	54 infants (2 twin pregnancies)
Spontaneous abortion	10
Therapeutic abortion	6
Obstetric complications	4/50 (17%)
Hypertensive disorders of pregnancy (preeclampsia, gestational hypertension)	4
Gestational diabetes	2
Placenta praevia	1
Placentomegaly	1
Birth weight (g) (singletons only, n = 48)	2,714 ± 709 (range 964–4,309)
Birth weight <2,500 g	15/48 (31%)
GA (wks) (singletons only)	36.7 ± 3.6 (range 24–41)
Preterm delivery (<37 wks GA)	19 (39%)
Very preterm delivery (<34 wks GA)	9 (18%)
Induction of labor	20/48 (42%)
Cardiac reasons	14
Obstetric reasons	6
Cesarean section	15/52 (28%)
Cardiac reasons	8
Obstetric reasons	7
Obstetrical anesthesia	
Epidural	44/52 (85%)
Spinal	3 (6%)
General	4 (8%)
None	1 (2%)
Digitalis or afterload reduction	17/49 (35%)
Antiarrhythmic drug in pregnancy	10/50 (20%)
CCU/ICU admission	8/49 (17%)
Length of stay for delivery (d)	6.2 ± 5.1 (range 2–21)
Last known functional class after pregnancy	
NYHA functional class I	24/33 (72%)
NYHA functional class II	6/33 (18%)
NYHA functional class III	3/33 (9%)

CCU = coronary care unit; GA = gestational age; ICU = intensive care unit; NYHA = New York Heart Association.

Pregnancy outcomes: Of the 70 pregnancies, 54 (78%) resulted in 56 live births, which included 2 twin pregnancies. There were 10 spontaneous abortions and 6 therapeutic abortions; 2 of the therapeutic abortions were for perceived cardiac risk. This rate of spontaneous abortion (14%) did not exceed that for the population (p = NS). The mean gestational age at delivery for singleton pregnancies was <37 weeks (36.7 ± 3.6, range 24 to 41). Table 2 lists maternal and fetal outcomes; complete details were not available for all pregnancies.

There were no reported congenital anomalies or cardiac defects, although 1 child who demonstrated developmental

delay was later diagnosed with cerebral palsy. All others are alive and well.

Slightly fewer than half of the women had induction of labor, most of these for cardiac causes. Fourteen of the pregnancies (28%) were delivered by cesarean section; of these, 6 were performed for obstetric indications and 8 for cardiac indications.

Overall, 39% of infants were born prematurely at <37 weeks gestation, and 9 of these infants (18%) were born at <34 weeks (Table 2). Compared with the 2000 United States overall rate of prematurity of 11.6%,[1] these women with dextro-TGAs had a significantly higher rate of prematurity than expected ($p < 0.025$). Birth weight in singletons averaged 2,714 ± 709 g (range 964 to 4,309); 15 of these infants (31%) weighed <2,500 g. Again, this rate of low birth weight was significantly greater than the expected 2000 United States rate of 7.6% ($p < 0.01$).

Cardiac complications in pregnancy: Cardiac complications occurred in 19 of the 53 pregnancies (36%) for which information was available. Of the 40 women who became pregnant, 18 (45%) experienced cardiac complications in ≥1 pregnancy; 1 woman experienced a cardiac complication in 2 pregnancies (atrial fibrillation). In 11 pregnancies, the cardiac complications occurred in the third trimester of pregnancy; this occurred intrapartum in 1 woman and postpartum in 6 women. During pregnancy, 6 women developed heart failure beginning from 30 to 33 weeks of gestation. In 4 of these women, emergency delivery was required at <34 weeks of gestation (unknown in 1 woman). One of these women died suddenly at 6 weeks postpartum, and another was evaluated for cardiac transplantation. Atrial flutter or fibrillation developed in 5 women almost exclusively in the third trimester; 2 of these women also developed heart failure. Intrapartum, 1 woman developed atrial flutter as well. Last, hemoptysis developed in 2 women in the second and third trimesters. During pregnancy, 35% of patients for whom data were available received digitalis or afterload reduction in pregnancy, and 20% received antiarrhythmic drugs.

Postpartum, cardiac events developed in 7 women who had uncomplicated pregnancies. In 5 women, congestive heart failure developed 2 to 9 days postpartum. In 3 of these 5 women, severe failure was evident. One of these women was hospitalized until cardiac transplantation. A new atrial baffle leak developed in 1 woman after delivery and was evidenced by decreased oxygen saturation. Last, 1 woman developed atrial fibrillation 1 day postpartum. One woman, who had experienced 4 pregnancies (1 twin), developed signs of failure and flutter after her second pregnancy, which was electively terminated. After her fourth delivery, she became progressively more debilitated and 3 years after delivery was being evaluated for transplantation but died suddenly.

The length of hospital stay for labor and delivery for all women in the study was 6.2 ± 5.1 days (range 2 to 21). Seven women (16%) were admitted to the intensive care unit or coronary care unit after delivery.

Obstetric complications occurred in 7 of the 51 pregnancies (14%) for which this information was available. Four women developed preeclampsia or gestational hypertension, 2 developed gestational diabetes, and 1 each had placenta praevia and placentomegaly (with preeclampsia).

Predictors of cardiac complications in pregnancy: We assessed patient risk factors in the 19 pregnancies complicated by cardiac events. Comparing variables associated with the 19 pregnancies with cardiac complications and in the 33 pregnancies without, there were no statistically significant differences in the type of surgical repair, age at repair, the presence of other heart defects; functional class before pregnancy; the presence of atrioventricular block, arrhythmia, or type of pacemaker; or RV dysfunction, tricuspid insufficiency, or arrhythmias identified before pregnancy. However, the occurrence of reoperation for dextro-TGA was related to having a cardiac event; significantly more women who had cardiac complications had reoperations, whereas no women with normal pregnancies required reoperations ($p = 0.004$). Similarly, significantly more women were taking cardiac medications before pregnancy in the group of women who developed cardiac complications compared with those women who did not. Gestational age and birth weight were not significantly affected by the occurrence of a cardiac event.

Discussion

Survival rates for patients surgically treated with the atrial Mustard procedure for simple TGA have been reported to be 84% to 91% at 10 to 30 years for simple TGA. The survival rate for the Senning procedure has been reported to be 95.7% at 20 years.[2] For patients with complex TGA, 10- to 25-year survival rates were 76% to 86% with Mustard repair and 63% to 84% with Senning repair.[3–5] However, despite favorable survival rates, a number of long-term problems are known to be associated with the Mustard procedure. These include systemic RV failure, tricuspid regurgitation, sinus node dysfunction, arrhythmias, and pulmonary venous or systemic venous baffle obstruction. A better understanding of these variables is important in determining what added risk the physiologic burden of a normal pregnancy might bring to women after the atrial repair of TGA.

Systemic ventricular (RV) function has long been a concern for these patients. The concern centers on a morphologic right ventricle's ability to sustain function as a systemic pump over an extended period of time and to be able to respond normally to increased workloads such as occur during pregnancy. Abnormal RV ejection fractions at rest and with exercise in patients with TGA after atrial repair have been reported by a number of different investigators.[6–12] However, comparing groups of patients who underwent atrial repair, Graham et al[13] found improved post-

operative RV ejection fractions in patients operated on after 1974, suggesting that this RV dysfunction may be due to age at surgery and operative techniques, particularly myocardial protection. In this current series, the initial surgeries were performed from 1967 to 1984, at a mean age of 21 months, but there were no differences between age at surgery between those who did and those who did not develop RV failure.

Tricuspid incompetence, a common finding, is usually found to be of a mild degree. It is more problematic in patients who have undergone ventricular septal defect repair. In our series, no patient was found to have greater than mild tricuspid regurgitation at the onset of her pregnancy, and it was not a factor in those women who developed heart failure.

Despite laboratory evidence for RV systolic and diastolic dysfunction,[14] most young adults continue to lead relatively normal lives after atrial repair.[15] The onset of clinical congestive heart failure, however, does occur in as many as 22% of adults after Mustard repair followed longitudinally.[16] Further evidence for the progressive deterioration of systemic RV function with advancing age is found in the report by Graham et al,[17] showing that 67% of patients with congenital corrected TGA and associated lesions and 25% of patients with congenital corrected TGA and no associated lesions developed congestive heart failure by 45 years of age. Although systemic RV dysfunction may be more prevalent in patients beyond the usual childbearing years, a major questions remains as to whether pregnancy can accelerate this process.

Abnormalities in rate and rhythm have been ascribed to the result of sinus node damage and subsequent reduction in automaticity.[18] The most common problem is sinus node dysfunction resulting in junctional bradycardia.[19,20] More serious is the onset of atrial flutter, supraventricular tachycardia, or atrioventricular node dysfunction.[20,21] Although these problems are believed to be due to operative techniques, changes in procedures have not markedly changed the long-term outlook for developing arrhythmias. It has been suggested that the late onset of arrhythmia may be a surrogate marker for RV dysfunction.[12]

Although not strongly demonstrated in this series, the catecholamine or sympathetic stimulation associated with delivery may induce rhythm disorders, as was the case in the 1 woman who developed atrial flutter during labor. Of further potential concern is the postpartum sudden death reported herein. This tragic complication can occur in up to 4% of patients followed longitudinally after the atrial repair of TGA.[22]

Although the data presented represent 1 of the largest clinical series reported on pregnancy outcomes after atrial baffle repair for TGA, there are a number of limitations to the study. Because our method of enrollment did not mandate that all patients followed in their participating centers be enrolled, we cannot be certain that our data are all inclusive. We did, however, ask that all patients from each center who met entry criteria be enrolled. Additionally, because of the retrospective nature of the study, the inclusion of data such as prepregnancy and postpartum echocardiographic studies were not available on all subjects.

Despite these limitations, this study demonstrates the potential deleterious effects of pregnancy in women with TGA who have had reoperations before pregnancy and/or were receiving cardiac medications before pregnancy. Although there was no difference in the occurrence of cardiac complications in women with or without RV dysfunction, tricuspid regurgitation, or arrhythmia before pregnancy, we can speculate that these variables might be predictive of poorer outcomes with a larger cohort of patients, stressing the importance of collaboration between high-risk perinatologists and cardiologists experienced in the care of patients with congenital heart disease.

Appendix

The participating centers and their representatives are as follows: Dr. William Albers, St. Francis Medical Center, Peoria, Illinois; Dr. Beth Brickner, University of Southwestern Medical School, Division of Cardiology, Dallas, Texas; Dr. Phillip Brook and Kathryn Junge, RN, BSN, Washington University School of Medicine, Cardiovascular Division, St. Louis, Missouri; John S. Child, MD, and Joseph K. Perloff, MD, Ahmanson/UCLA Adult Congenital Heart Disease Center, Los Angeles, California; Dr. William Davidson, Adult Congenital Heart Disease Program, Penn State University, Hershey, Pennsylvania; Nancy Drucker, MD, Vermont/New Hampshire Regional Program in Pediatric Cardiology, University of Vermont, Burlington, Vermont; Thomas Graham, MD, Vanderbilt University Medical Center, Division of Pediatric Cardiology, Nashville, Tennessee; John D. Kugler, MD, and Jenny Strawn, RN, Children's Hospital, Pediatric Cardiology, Omaha, Nebraska; Michael J. Landzberg, MD, and Susan Fernandez, PA-C, Boston Children's Hospital, Boston, Massachusetts; Marla Mendolsohn, MD, Adult Congenital Heart Program, Northwestern, Chicago, Illinois; Richard Meyer, MD, Children's Hospital Medical Center, Cincinnati, Ohio; Cynthia Morris, PhD, MPH, Oregon Health Sciences Medical Center, Portland, Oregon; Mark Perlroth, MD, Stanford University School of Medicine, Stanford, California; Pate Thomson, MD, and Sally Higgins, PhD, RN, CNS, Alta Bates, Oakland, California; Susan Willansky, MD, St. Luke's Hospital, Houston, Texas; and Tom Zellers, MD, and David Fixler, MD, Dallas Children's Hospital, Dallas, Texas.

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