Impact of Pregnancy on the Systemic Right Ventricle After a Mustard Operation for Transposition of the Great Arteries

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OBJECTIVES
We sought to determine the impact of pregnancy on the systemic right ventricle (RV) after a Mustard operation for transposition of the great arteries.

BACKGROUND
Dysfunction of the RV remains a continuing problem after a Mustard operation. Concerns exist about the potentially deleterious effects of pregnancy on this ventricle.

METHODS
The records of 16 women who completed 28 pregnancies were reviewed for clinical status, echocardiographic evaluation of RV dimensions, RV function, and tricuspid regurgitation (TR) before, during, and after pregnancy.

RESULTS
Women were in New York Heart Association functional class I (n = 21) and II (n = 7) before pregnancy. The functional class deteriorated in six women, with no return to the pre-pregnancy level after delivery in two. Data on RV dimensions were available in 18 pregnancies, on RV function in 21, and on TR in 20. Before pregnancy, RV dilation was absent (n = 4), mild/moderate (n = 12), or severe (n = 2) and progressed in five women (31%), with no recovery in all patients at the last follow-up. Right ventricular systolic dysfunction was absent (n = 16), mild/moderate (n = 4), or severe (n = 1) before pregnancy and progressed in four women (25%), with no recovery in three cases. Tricuspid regurgitation was absent (n = 8), mild (n = 9), or moderate (n = 3) before pregnancy and deteriorated in eight women (50%), with no recovery in three patients.

CONCLUSIONS
Pregnancy after a Mustard operation is clinically well tolerated but carries a risk of RV dysfunction, which is sometimes irreversible. (J Am Coll Cardiol 2004;44:433–7) © 2004 by the American College of Cardiology Foundation

Transposition of the great arteries (TGA) is a complex cardiac malformation that carried a mortality rate of >90% in the first year of life, before the introduction of the intra-atrial baffle operation. This type of repair restores normal circulation and improves survival but is associated, in the long term, with dilation of the systemic right ventricle (RV) and, in some cases, with RV systolic dysfunction (1–3). Even if most patients report that they are asymptomatic at usual levels of activities 20 or more years after repair (3–5), a reduction in their exercise capacity has been well documented (3–8). As many women who underwent a Mustard operation in infancy are now reaching their reproductive age, concerns exist about the potential deleterious short- and long-term effects of pregnancy on the systemic RV. The aim of this study was to determine the impact of pregnancy on the systemic RV in women with TGA after a Mustard operation.

METHODS
The records of all female patients who had a Mustard operation for TGA and are followed at the Adult Congenital Heart Center of a tertiary hospital were reviewed. Their clinical status, need for cardiovascular medication, presence of arrhythmias, and number of pregnancies were noted. The echocardiographic reports were reviewed for RV dimensions, RV systolic function, and the degree of tricuspid regurgitation (TR). The RV dimensions were qualitatively evaluated as normal, mildly to moderately dilated, or severely dilated. Right ventricular systolic dysfunction was also qualitatively assessed as absent, mild to moderate, or severe. The degree of TR was qualitatively assessed by color Doppler imaging. Maternal complications and fetal outcome were noted. Continuous data are presented as the mean value ± SD.

RESULTS
Patient population. Of the 24 women followed at our center, 16 had a total of 28 pregnancies: 9 had one pregnancy, 3 had two, 3 had three, and 1 had four. All patients had TGA with an intact ventricular septum. The mean age at the time of the Mustard operation was 43 ± 25 months (range 18 to 108), and the mean age at pregnancy was 27 ± 5 years (range 19 to 37). The mean interval between the Mustard repair and the first pregnancy was 21 ± 4 years (range 14 to 30). All women were in New York Heart Association (NYHA) functional class I (n = 21) or II (n = 7) before their pregnancies. Five women

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had at least one episode of supraventricular tachyarrhythmia, and five had implantation of a permanent pacemaker for sick sinus syndrome before pregnancy. Patients were taking a cardiovascular medication before 15 pregnancies: angiotensin-converting enzyme (ACE) inhibitors (n = 3), angiotensin II receptor blockers (n = 6), methyldopa (n = 1), diuretics (n = 2), digoxin (n = 12), aspirin (n = 4), and amiodarone (n = 1). All medications were stopped at the diagnosis of pregnancy, except for digoxin in three cases and aspirin in two. Clinical follow-up after the last pregnancy ranged from 2 to 120 months (mean 31 ± 32) and after the Mustard operation from 20 to 36 years (mean 27 ± 5).

**Clinical status.** There was no maternal death. Six women (38%) had deterioration of their NYHA functional class during seven pregnancies (Table 1). This deterioration occurred during a first pregnancy in four cases, during a second in one, and during a third in two. At the last follow-up, all patients went back to their pre-pregnancy functional class, except for two (Patient #12, second pregnancy; Patient #13, third pregnancy). Two patients had arrhythmias during pregnancy: one had junctional bradycardia requiring a permanent pacemaker after delivery and one had supraventricular tachycardia for which no treatment was needed. Three patients had gestational diabetes, and one developed mild hypertension.

**Echocardiographic evaluation.** At baseline, one patient had complete occlusion of her superior baffle, but none had a significant intracardiac shunt or other residual lesions.

Echocardiographic data on the systemic RV dimensions were available in 18 pregnancies, with a mean follow-up after pregnancy of 24.1 ± 20.0 months (range 2 to 65). Five women (31%) had progression of their RV dimensions during seven pregnancies (Table 1). This progression in RV size was noted during or after a first pregnancy in four cases, a second in one, and a third in two. Two patients (Patients #10 and 14) had progression of RV dimensions with return to the baseline level after a first pregnancy, and both of them had further dilation with no recovery in subsequent pregnancies. At the last follow-up, the RV dimensions of these five women remained greater than before pregnancy.

Echocardiographic data on systemic RV function were available in 21 pregnancies, with a mean follow-up after pregnancy of 32.6 ± 34.0 months (range 2 to 120).

### Table 1. Clinical and Echocardiographic Data Before, During, and After Pregnancy

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A = absent; M/M = mild to moderate; Mod. = moderate; NYHA = New York Heart Association; Pt. = patient; RV = right ventricle; S = severe; TR = tricuspid regurgitation.
women (25%) had deterioration of their RV systolic function during four pregnancies (Table 1). This deterioration was noted during a first pregnancy in two cases and during a second in two. In three of these cases, deterioration of RV function was associated with progression of RV dilatation. At the last follow-up, three patients (75%) did not recover to the baseline level.

Data on the degree of TR were available in 20 pregnancies, with a mean follow-up after pregnancy of 31.5 ± 33.1 months (range 2 to 120). Eight women (50%) had progression in the degree of TR during or after nine pregnancies (Table 1). This occurred during or after a first pregnancy in five cases, a second in three, and a third in one. At the last follow-up, the degree of TR returned to the baseline level in five women (63%) but did not recover in three (37%).

**Clinical heart failure.** Two of the 16 women required heart failure therapy during or soon after pregnancy. A 27-year-old woman (Patient #7) in NYHA class II with severe RV dilatation, mild systolic dysfunction, and mild TR presented with a deterioration of functional class during a first pregnancy but did not require medication. Echocardiographic data remained unchanged during her pregnancy. Six months after pregnancy, she went back to NYHA class II but had progression of TR (from mild to moderate). This was associated with episodes of atrial flutter. She was then put on ACE inhibitors, sotalol, and warfarin.

A 22-year-old woman (Patient #14) in NYHA class II with normal RV dimensions, normal systolic function, and mild TR presented mild RV dilatation during a first pregnancy. Follow-up echocardiograms over the next five years showed progressive systolic dysfunction (from normal to mild). She had a second pregnancy at age 31 years, with progression of the degree of TR (from mild to moderate). A third pregnancy occurred four months after delivery. During this last pregnancy, she had to be hospitalized at 28 weeks of gestation for progressive dyspnea and fatigue requiring furosemide and hydralazine. An echocardiographic evaluation showed severe RV dilatation, moderate systolic dysfunction, and moderate TR. She remained stable at rest in the hospital, and an elective cesarean section was performed at 36 weeks of gestation. Six months after delivery, the patient was in NYHA class II while taking diuretics and ACE inhibitors, with no improvement in her echocardiographic parameters.

**Obstetrical history and fetal outcome.** Obstetrical data were available in 18 pregnancies. Delivery occurred at a mean of 38.1 ± 1.5 weeks, with an induction rate of 73% and a cesarean section rate of 17% (3 of 18 pregnancies). The cesarean sections were performed for obstetrical reasons in two cases and for a heart condition in the patient who required heart failure therapy during pregnancy. The mean birth weight was 3,040 ± 540 g, and no infant had a congenital heart defect or other adverse event.

**Women with no pregnancy.** Eight women did not experience a pregnancy, and their age ranged from 12 to 72 months (mean 33) at time of the Mustard operation. Two women died suddenly. A 21-year-old woman with severe RV dilatation and dysfunction who never had arrhythmias died suddenly at work. She had been advised against pregnancy because of severe systemic RV dysfunction and poor exercise tolerance. A 27-year-old woman in NYHA class III with severe TR, severe RV systolic dysfunction, and obstruction of the superior vena cava baffles underwent surgical repair of the obstructed baffles and tricuspid valve replacement. She died suddenly one week after hospital discharge, and the autopsy showed a major acute postero-septal myocardial infarction with RV involvement and a nonfunctional tricuspid prosthetic valve covered with thrombus.

The six survivors were in NYHA class I (n = 1) or II (n = 5) at 18 to 32 years (mean 24 ± 5) after the Mustard operation. Two women had been treated for supraventricular arrhythmias, three required a permanent pacemaker, and two were taking a cardiovascular medication (digoxin and angiotensin II receptor blockers in one and sotalol in the other). The last echocardiographic evaluation showed RV dilatation (mild to moderate in five and severe in one), RV dysfunction (absent in three, mild to moderate in two, and severe in one) and TR (mild in six). Two patients were taking oral contraceptive pills, and three had a tubal ligation. One of the latter patients underwent reversal of her tubal ligation in order to become pregnant.

**DISCUSSION**

Dilation and failure of the systemic RV associated or not with TR remains a continuing problem in patients who underwent an intra-atrial correction for TGA, even if the vast majority of these adults are asymptomatic and able to lead normal and fulfilling lives (2–4). Women who had this type of repair in their childbearing years now go through pregnancy in increasing numbers, but because of the relative rarity of the disease, little is known about the short- and medium-term impact of pregnancy on the systemic RV. This study is the largest, to our knowledge, to look at the impact of pregnancy on the systemic RV.

Pregnancy imposes an increasing, sustained hemodynamic burden on these patients, the consequences of which have not been well studied. During pregnancy, there is a 40% to 50% increase in blood volume, and the heart rate increases by about 10 to 20 beats/min. There is also a decrease in systemic and pulmonary vascular resistance. All these changes result in a 30% to 50% increase in cardiac output, with a maximum rise around 32 weeks of gestation (9). However, the systolic function that is preserved throughout most of pregnancy diminishes near term and early postpartum because of decreased contractility and reduced preload (10). During a normal pregnancy in a healthy woman, all cardiac chamber dimensions increase on echocardiography, with an augmentation of ~20% in the size of the right atrium and RV, 12% in the size of the left atrium, and 6% in the size of the left ventricle (11,12). A
mild progression in valve regurgitation can be present, but all these modifications return to the baseline level after delivery.

In case reports and small series of up to 11 pregnancies (13–21) looking at the outcome of pregnancy in asymptomatic or mildly symptomatic women after an intra-atrial baffle repair, the authors have described symptomatic heart failure requiring therapy during pregnancy (13,14,16,17,19–21), deterioration in RV systolic function (13,14,16,19,20), development of supraventricular arrhythmias (13,14,18,21), stroke (21), and death (20,21). These results, like our data, confirm that pregnancy after a Mustard operation can be successful but carries a risk of deterioration in functional class, even in women who are asymptomatic before pregnancy. In these reports, there was no systematic echocardiographic assessment of the RV.

Clarkson et al. (22) reported the clinical outcome of 15 pregnancies in nine asymptomatic women who remained free of cardiac symptoms during or after pregnancy. In this series, echocardiographic data were available in three pregnancies, and the authors noted an increase in RV volumes by 31 to 32 weeks of gestation. Volumes decreased eight to 11 weeks postpartum but remained greater than those in early pregnancy. There were no significant changes in ejection fraction or the degree of TR. The data from these three patients are confirmed in our study, which shows that the volume overload of pregnancy is associated with an increase in RV dimensions.

The fact that some women may experience worsening of their functional class during or immediately after pregnancy could be related to many factors. The observed increase in the size of the systemic ventricle that accompanies a normal pregnancy may, in this particular case, increase the regurgitation of a tricuspid valve functioning at systemic pressure, with an ensuing increase in left atrial pressure. The authors have shown that patients who underwent a Mustard procedure sometimes fail to increase their cardiac output with exercise, a fact that has been variously attributed to impaired contractility, chronotropic incompetence, or impaired atrioventricular transport secondary to the abnormal intra-atrial pathways (6,23,24). With the physiologic changes of pregnancy being similar to the ones observed during exercise but occurring over an extended period, the incapacity to increase cardiac output may explain the clinical deterioration observed in some patients.

As pregnancy after a Mustard operation is clinically well tolerated, it seems reasonable not to discourage women from going through a pregnancy if they have a good functional class, good exercise capacity, and normal or near normal RV systolic function. These women must, however, be made aware of the possibility of RV dysfunction occurring with pregnancy, and that this deterioration may occur at their first pregnancy, even if they are asymptomatic, and that it might not be reversible after delivery. The long-term impact of the changes that could occur during pregnancy remains unknown, and close clinical and echocardiographic follow-up should be maintained in the months after delivery. In symptomatic women with poor systemic RV function, pregnancy should probably be discouraged.

**Study limitations.** Because of the retrospective nature of the study, some echocardiographic data were unavailable or not routinely performed at the time of pregnancy. We had to rely on qualitative assessment of the RV dimensions and function, but 75% of the echocardiograms were performed by the same two echocardiographers (Drs. Mercier and Dore). As systemic ventricular dysfunction can progress in all patients with a Mustard procedure, it cannot be excluded that part of the deterioration observed during pregnancy was related to the natural history of the disease. However, the relatively short follow-up period makes this improbable.

**Conclusions.** Pregnancy after a Mustard operation can be clinically successful but carries a risk of RV dysfunction that is sometimes irreversible. Further studies are needed to evaluate the long-term impact of pregnancy on the systemic RV. In the meantime, close collaboration between cardiologists with expertise in congenital heart disease, obstetricians, and anesthesiologists is essential to ensure appropriate counselling before and adequate follow-up during and after pregnancy.

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