

# Pregnancy Outcomes Following Cardiac Transplantation

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## Abstract

**Objective:** This study sought to report pregnancy outcomes in women following cardiac transplantation.

**Methods:** This was a descriptive retrospective cohort study of women with pregnancies following cardiac transplantation managed at two large tertiary centres in Canada and Belgium between 2001 and 2017.

**Results:** Sixteen women had 17 singleton pregnancies following cardiac transplantation. The mean maternal age was  $28 \pm 5.8$ , and the transplant-to-pregnancy interval was  $7.3 \pm 4.0$  years. There were two first trimester terminations, one for teratogenicity concerns and the other because of a maternal cardiac condition. There was one spontaneous miscarriage. All women had normal left ventricular function at the start of pregnancy. Graft rejection occurred in two women. Other maternal complications included anemia requiring blood transfusion ( $n = 5$ ), renal failure or deterioration ( $n = 4$ ), preeclampsia ( $n = 2$ ), and urine infections ( $n = 2$ ). The mean GA at delivery was  $35 \pm 3.5$  weeks. Six infants were born preterm, and two were small-for-gestational-age. Fetal anomalies were identified in two pregnancies. Women were followed after pregnancy for a median of 5.6 years (range, 10 months to 15 years). Although there were no deaths during pregnancy, two women died at 10 and 18 months after delivery.

**Conclusion:** With appropriate multidisciplinary care, women with cardiac transplants can have successful pregnancies. Although rates of fetal loss are low, these women continue to be at risk for graft rejection, preterm birth, other pregnancy-related complications, and cardiovascular death.

**Key Words:** Cardiac transplantation, pregnancy, outcomes, management, pregnancy complications

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## Résumé

**Objectif :** Cette étude avait pour but d'examiner les issues de grossesse chez les femmes ayant subi une transplantation cardiaque.

**Méthodologie :** Cette étude de cohorte rétrospective descriptive porte sur des femmes enceintes ayant subi une transplantation cardiaque et ayant été prises en charge dans deux grands centres de soins tertiaires du Canada et de la Belgique entre 2001 et 2017.

**Résultats :** Seize femmes ayant subi une transplantation cardiaque ont eu un total de 17 grossesses monofœtales. L'âge maternel moyen était de  $28 \pm 5,8$  ans, et le temps moyen écoulé entre la greffe et la grossesse était de  $7,3 \pm 4,0$  ans. Deux grossesses ont été interrompues au premier trimestre : l'une en raison d'une possible tératogénèse et l'autre en raison de troubles cardiaques chez la mère. Une grossesse s'est soldée par une fausse couche. Toutes les femmes présentaient une fonction ventriculaire gauche normale en début de grossesse. Un rejet du greffon est survenu chez deux femmes. Les autres complications maternelles comprenaient notamment une anémie ayant nécessité une transfusion sanguine ( $n = 5$ ), une détérioration de la fonction rénale ou une insuffisance rénale ( $n = 4$ ), une prééclampsie ( $n = 2$ ) et des infections urinaires ( $n = 2$ ). L'âge gestationnel moyen à l'accouchement était de  $35 \pm 3,5$  semaines. Six bébés sont nés prématurés, et deux étaient petits pour leur âge gestationnel. Des anomalies fœtales ont été observées dans deux grossesses. Les femmes ont toutes été suivies après leur grossesse pendant une durée médiane de 5,6 ans (étendue : 10 mois à 15 ans). Bien qu'il n'y ait eu aucun décès maternel à l'accouchement, deux femmes sont décédées 10 et 18 mois plus tard.

**Conclusion :** Les femmes ayant subi une transplantation cardiaque peuvent avoir une grossesse réussie si elles reçoivent les soins multidisciplinaires appropriés. Même si le taux de décès fœtal était faible, ces femmes sont exposées à un risque de rejet du greffon, d'accouchement prématuré, d'autres complications liées à la grossesse et de décès d'origine cardiovasculaire.

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## INTRODUCTION

There have been a number of reports of pregnancies following cardiac transplantation since the first publication in 1988.<sup>1</sup> These pregnancies are not without risks to the mother and the baby, and therefore, the International Society of Heart and Lung Transplantation (ISHLT) recommends management by a multidisciplinary team involving a cardiologist, transplant specialist, high-risk obstetrician, obstetric anaesthesiologist, neonatologist, and appropriate support staff with expertise in the management of pregnant women with complex cardiac disease.<sup>2</sup> Currently there is only one active registry reporting pregnancy outcomes in women with solid-organ transplants, the National Transplantation Pregnancy Registry in the United States, and the numbers of cardiac transplant recipients are limited.<sup>3</sup> Data obtained from small case series<sup>4-8</sup> have been important in informing the management of pregnancies in women with cardiac transplantation. This paper reports the experience in the management of pregnant women with cardiac transplants at two large tertiary care centres in Canada and Belgium.

## MATERIAL AND METHODS

All consecutive women with pregnancies following cardiac transplantation who attended the antenatal clinics at Mount Sinai Hospital, Toronto and University Hospitals, Leuven, Belgium between 2001 and 2017 were identified, and their medical records were reviewed. Baseline data obtained included the following: maternal demographics; prior obstetric history; details pertaining to the cardiac transplantation and graft health, including the date of transplantation, indication for transplantation, history of graft rejection, immunosuppressive therapy, and cardiac function at the onset of pregnancy; and details on the current pregnancy, including whether the pregnancy was conceived spontaneously or by assisted reproductive techniques.

Maternal cardiac, obstetric, and fetal or neonatal complications during pregnancy were examined. Maternal adverse events included cardiac death, heart failure, sustained arrhythmias, graft rejection or failure, and renal dysfunction, which was defined as a 30% increase in serum creatinine levels over baseline. Obstetric outcomes examined included miscarriage, gestational age (GA) at delivery, mode of delivery, preeclampsia, and postpartum hemorrhage. Perinatal outcomes included preterm births, small-for-gestational-age (SGA) infants (under the tenth centile for GA and sex), congenital malformations, and if possible results from placental histopathological examination. Late survival after pregnancy was obtained by chart review.

Results were presented as means and standard deviations, ranges, and proportions. This study was approved by the Research Ethics Boards of both institutions.

## RESULTS

### Maternal Characteristics

We identified 16 women who had a total of 17 pregnancies following cardiac transplantation. The baseline maternal characteristics are described in Table 1. The mean maternal age was  $28 \pm 5.8$  years, and all were singleton pregnancies. One was conceived by assisted reproductive techniques, whereas the remainder were spontaneously conceived. The mean time between cardiac transplantation and pregnancy was  $7.3 \pm 4.0$  years. Indications for cardiac transplantation were cardiomyopathy ( $n = 10$ ) and complex congenital heart disease ( $n = 6$ ).

Five women had a history of graft rejection before conception, and one experienced graft loss requiring repeat cardiac transplantation. All had normal left ventricular function at the start of pregnancy. All women were receiving calcineurin inhibitors (tacrolimus or cyclosporine), and nine of these women were also taking prednisone (5–10 mg daily). In addition, five were also taking azathioprine, three were taking mycophenolate mofetil (MMF), and two were taking

**Table 1. Baseline maternal characteristics**

Maternal characteristics (n = 17)	c (%) or mean $\pm$ SD
Age at conception in years, mean $\pm$ SD	28 $\pm$ 5.8
Transplant-to-pregnancy interval in years, mean $\pm$ SD	7.3 $\pm$ 4.0
Abnormal left ventricular systolic function at conception, n (%)	0/17 (0)
Nulliparous, n (%)	11/17 (64.7)
Assisted reproductive techniques, n (%)	1/17 (5.9)
Singleton pregnancy, n (%)	17/17 (100)
Immunosuppressive treatment at the start of pregnancy, n	
• Tacrolimus + steroids	6
• Tacrolimus + steroids + azathioprine	2
• Tacrolimus + azathioprine	2
• Tacrolimus + mycophenolate mofetil <sup>a</sup> + steroids	2
• Tacrolimus alone	1
• Tacrolimus + mycophenolate mofetil <sup>a</sup> + sirolimus <sup>a</sup>	1
• Tacrolimus + sirolimus + steroids	1
• Cyclosporine + azathioprine + steroids	1
• Cyclosporine + steroids	1

<sup>a</sup>Stopped early in pregnancy.

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