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Management of pregnancy in the post-cardiac transplant patient



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ABSTRACT

Over the past 10 years, heart transplantation survival has increased among transplant recipients. Because of improved outcomes in both congenital and adult transplant recipients, the number of male and female patients of childbearing age who desire pregnancy has also increased within this population. While there have been many successful pregnancies in post-cardiac transplant patients reported in the literature, long-term outcome data is limited. Decisions regarding the optimal timing and management of pregnancy in male and female post-cardiac transplant patients are challenging and should be coordinated by a multidisciplinary team of healthcare providers. Pregnant patients will need to be counseled and monitored carefully for complications including rejection, graft dysfunction, and infection. This review focuses on preconception counseling for both male and female cardiac transplant recipients. The maternal and fetal risks during pregnancy and the postpartum period, including risks to the fetus fathered by a male cardiac transplant recipient will be reviewed. It also provides a brief summary of our own transplant experience and recommendations for overall management of pregnancy in the post-cardiac transplant recipient.

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Introduction

The first pregnancy and delivery post-solid organ transplant occurred in 1958 in a renal transplant recipient.^{1,2} In 1988, the first pregnancy in a post-cardiac transplant patient was reported in a female patient with a history of a dilated cardiomyopathy who conceived less than 2 years post-transplant.^{1,3,4} Since then, data published in case reports along with outcomes data from the National Transplantation Pregnancy Registry (NTPR) have demonstrated many successful pregnancies in solid organ transplant recipients including in cardiac transplant patients.^{3,5–11}

Worldwide, female patients represent approximately 20% of overall cardiac transplants.¹² Between 2006 and 2012, 25%

of female cardiac transplant patients were between the ages of 18 and 39 years and were of childbearing age.¹² Females are also part of the growing population of surviving congenital cardiac transplant recipients. As this population ages, the number of female patients of childbearing age who desire pregnancy will also increase. As a result, healthcare providers should be familiar with the maternal and fetal risks associated with pregnancy in general, including risks to the fetus fathered by a male cardiac transplant recipient, as well as understanding the unique management challenges during pregnancy that arise while caring for a cardiac transplant recipient. These include assessment of graft function, rejection, immunosuppressive medications, and infection. Integration of this information by healthcare providers as part of

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a multidisciplinary care plan is essential in order to provide the patient an adequate assessment of overall risk and appropriate care throughout pregnancy and the postpartum period.

Preconception counseling and baseline risk assessment

Ideally, preconception counseling should begin in all patients during their pre-transplant evaluation and throughout their post-transplant care.¹³ Pre-transplant, pregnancy is contraindicated in women with stage D heart failure due to the increase in the overall metabolic needs and increased hemodynamic load associated with pregnancy. Both women with stage D heart failure and those with advanced mechanical support devices such as left ventricular assist devices should be strongly counseled on birth control. Females with mechanical support devices are able to conceive and have had successful pregnancies. Two patients who conceived and delivered on mechanical support have previously been reported.^{14,15} In contrast, male patients with severe heart failure frequently are impotent, but implantation of mechanical support devices and subsequent cardiac transplantation can often ameliorate this problem, and these patients require genetic counseling for those with inherited cardiomyopathies.

In a cardiac transplant recipient, natural conception is a safe option. In vitro fertilization is also another option that has been successful in post-cardiac transplant patients.¹⁶ The International Society of Heart and Lung Transplantation (ISHLT) 2010 guidelines recommend the involvement of a multidisciplinary team of healthcare providers from transplant cardiology, maternal and fetal medicine, neonatology, psychology, genetics, and social services.¹⁷ If possible, the management plan should be coordinated at the cardiac transplant facility with the involvement of other members of the multidisciplinary team.

Preconception counseling should include assessment of overall risk to both mother and fetus. The patient should be counseled on the risk of pregnancy, specifically on the risk of acute rejection, graft dysfunction, infection, and the possible teratogenic effects of immunosuppressive medications. For female cardiac transplant recipients who consider pregnancy, the risk of allograft rejection during conception should be discussed. At our center, prior to conception, we request that fathers undergo human leukocyte antigen (HLA) testing. If the female cardiac transplant recipient's donor and the father share the same antigen, and particularly, if the recipient already has donor-specific antibodies to this HLA locus, then conception could provoke allograft rejection and the patient is counseled about the heightened risk to her graft.¹⁸ For male cardiac transplant recipients, there is no need for HLA testing in the mother.

The underlying etiology of the initial heart disease leading to transplant must be considered since certain transplant patients may require more detailed preconception counseling. A mother's pre-transplant diagnosis, especially of congenital heart disease or genetic disorders, can affect a child's outcome as well. Children of mothers with a pre-transplant diagnosis of congenital heart disease have up to a 10% risk of

congenital heart disease.^{4,19} As such, early fetal screening for congenital heart disease may be warranted in this population. Likewise, children born to mothers with a pre-transplant genetic condition are also at a higher risk for developing the same genetic disease.^{4,20,21} As such, transplant recipients need to be counseled on the risks of possible transmission of the disease to their unborn child. In our own transplant experience, a female patient with carnitine deficiency who subsequently underwent cardiac transplant at our center gave birth to twins with the same genetic condition. We recommend early referral and consultation with a genetic counselor in females with pre-transplant genetic conditions ideally prior to pregnancy.

It is unknown if female patients with a pre-transplant diagnosis of postpartum cardiomyopathy are at increased risk of recurrence of postpartum cardiomyopathy in the transplanted organ. These patients appear to be at increased risk of rejection within the first year post-transplant, and overall graft survival is shorter with an increased risk of retransplantation.²² Our policy has been to advise against pregnancy for patients with prior postpartum cardiomyopathy.

Timing of pregnancy

If a female cardiac transplant recipient chooses to conceive, then the patient is counseled to delay pregnancy until at least 1 year post-cardiac transplant and to expect more intense surveillance of graft function as the risk of rejection during pregnancy may be increased. If there is a high risk of rejection or baseline graft dysfunction is not adequate, pregnancy should be discouraged or delayed until these risks can be minimized.

While the ISHLT guidelines recommend that pregnancy should not be attempted less than 1 year post-cardiac transplant, several case reports have reported successful outcomes with varying time intervals from transplantation, some even as early as 3 months.^{10,23}

Cardiac assessment prior to conception

Baseline electrocardiogram and graft function should be assessed preconception since a successful pregnancy is most likely to occur in a cardiac transplant recipient with normal graft function and no evidence of rejection.^{8,10} If clinically indicated, dobutamine stress echocardiography or left and right heart catheterization with subsequent endomyocardial biopsy should be performed prior to pregnancy. If there is significant baseline graft dysfunction that would preclude a successful outcome, pregnancy should be discouraged.¹⁷ The hemodynamic changes associated with pregnancy, including an increase in cardiac output by as much as 30%, anemia, and volume expansion, are generally well tolerated in the post-cardiac transplant patient as long as there is adequate graft function.^{5,8,10,24}

Review of potential teratogenic immunosuppressive or other medications must be performed with a plan to alter these medications prior to pregnancy. Immunosuppressive medication

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