Transplant and ventricular assist devices: Gender differences in application and implementation

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Hear failure has reached epidemic proportions over the last several years. It may be no small coincidence that the incidence of obesity is also on the rise. Women tend to have a higher prevalence of heart failure over age 75. This may contribute to their relative underrepresentation as heart transplant and ventricular assist device (VAD) recipients. Total body surface area is also an issue with respect to certain VADs.

The most recent registry report of the International Society for Heart and Lung Transplantation (ISHLT) revealed that only 34.1% of donors were female.¹ The female heart donor in a female heart recipient may be responsible for an increased risk of interstitial myocardial fibrosis. As heart transplant recipients, women need a donor within 30% of their weight. A larger donor is indicated for the recipient with high pulmonary vascular resistance. Female recipients of cardiac transplantation have been reported to have an increased mortality when compared with male recipients.² Various immunologically related conditions, such as systemic lupus erythematosus and rheumatoid arthritis, are found in increased prevalence among women. Further, there is experimental evidence to suggest that fundamental immune responses, such as antibody production and rejection of allogeneic grafts, are potentiated in females. Thus, it is not surprising that studies have shown that female cardiac allograft recipients have a higher risk of cardiac rejection and the subsequent need for increased immunosuppression.³ How this affects survival in female patients remains to be seen. However, it certainly suggests that an earlier diagnosis and management of alloreactivity in female recipients before the development of acute rejection and the use of more focused and less global immunosuppressive therapy may significantly affect the outcome of female cardiac allograft recipients. Also, an increased risk of sensitization may be seen in multiparous females, especially when associated with placement of a left ventricular assist device (LVAD). Patients who are highly sensitized can be pretreated with intravenous immunoglobulin (IVIg) in preparation for heart transplantation.⁴ Cyclophosphamide is also given in addition to IVIg as part of the desensitization regimen.

As a woman progresses through life from neonate to elderly, certain interventional options for the treatment of heart failure are available. As a neonate, bridging to transplantation is done with extracorporeal membrane oxygenation (ECMO). The most common age for pediatric heart transplantation is now between 1 day and 1 year.⁵ With ECMO, there are no gender issues. Female subjects are well represented in a large review from the Deutsches Herzzentrum Berlin.⁶ They examined 95 children who underwent elective heart transplantation, emergency heart transplantation, and bridging to heart transplantation with a pulsatile pneumatic assist device. The group was 55 boys and 40 girls. Eighteen received a VAD and 8 of these were female. Gender did not affect survival, but a preoperative diagnosis of congenital heart disease did.

At the adolescent level, girls tend to react better to a heart transplant from an academic and social vantage point. Boys, however, do better physically. The adolescent who has viral myocarditis often undergoes implantation of an LVAD. The dramatic hemodynamic and physiologic improvement seen in this subgroup of patients makes them better candidates for a bridge to recovery and explant of the

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device. Young women tend to require heart transplantation for postpartum cardiomyopathy, myocarditis, or dilated cardiomyopathy. Postpartum cardiomyopathy may respond to unloading of the heart with a device and eventual device removal. As they leave childbearing years behind, more women have ischemic cardiomyopathy like their male counterparts, although at a somewhat older age. Women comprise only 22.4% of heart transplant recipients. Women have had children after heart transplantation. The increased plasma volume of pregnancy does stress a transplanted heart. Postmenopausal heart transplant recipients are at increased risk for osteoporosis. Weaning from steroids is helpful when appropriate.

Technically, heart transplantation in women is no different from that in men. If a complex reconstruction has been performed for congenital heart disease, transesophageal echocardiogram is a useful adjunct. The left atrial anastomosis is performed first, then the inferior vena caval anastomosis, the superior vena caval anastomosis, followed by the pulmonary arterial and aortic anastomoses. Care is taken to avoid narrowing either caval anastomosis or kinking of the pulmonary arterial anastomosis. Women tend to require transfusion more frequently than men after conventional heart surgery.⁷ This is probably also true after heart transplantation. Women with osteoporosis undergo sternal closure using figure-of-8 wire closure to reduce the incidence of sternal wound-related problems.

The results of the REMATCH trial (Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure) showed that in a randomized group of patients with class IV heart failure, those who received an LVAD had a 48% reduction in risk of death compared with the group receiving medical management.⁸ The type of VAD a woman receives is based on (1) size of patient, (2) degree of heart failure, and (3) whether or not she is a transplant candidate. The Novacor LVAD (Baxter Healthcare Corp, Novacor Div, Oakland, Calif) and Thoratec VE HeartMate LVAD (Thermo Cardiosystems, Inc, Woburn, Mass) require a body surface area of greater than 1.5 m². The Berlin Heart (Berlin Heart AG, Berlin, Germany) is extracorporeal and allows a lower body surface area. This is why it was used in children; however, it is not approved by the Food and Drug Administration. For patients with severe cardiogenic shock, an Abiomed (Abiomed, Inc, Danvers, Mass), Thoratec, or total artificial heart is used.⁹ These patients usually have right and left heart failure and some element of end organ failure. Patients with early decompensation of chronic congestive heart failure who are heart transplant recipients undergo placement of a HeartMate or Novacor VAD. Patients who are not transplant candidates, or who may recover heart function, receive an Abiomed, Thoratec, or centrifugal pump and are weaned within 1 week. Abiomed and centrifugal pumps can be a bridge to

another longer-term device, such as the Thoratec, HeartMate, or Novacor devices. In a very recent article, a 15-year experience is reported using the CardioWest total artificial heart (CardioWest Technologies, Inc, Tucson, Ariz) as a bridge to transplantation.¹⁰ Of the 127 patients, only 19 were women. Small body size was associated with increased operative mortality. Only 4 of 9 with a body surface area of less than 1.6 m² survived to transplantation. These smaller patients are better served with a biventricular pneumatic device (Thoratec).

Technically, women who are short, with not much length to their aortas, can be challenging recipients of a HeartMate or Novacor VAD. Circulatory arrest has even been used to deal with a lack of aorta when removing the VAD and performing the heart transplant. Smaller women have had difficulty with the abdominal placement of the pump. Previous left upper quadrant surgery or a long narrow rib cage can also contribute to difficulties intraoperatively, as well as to postoperative pain. Right ventricular dysfunction after LVAD insertion does not appear to be related to gender.¹¹

Quality of life issues are being evaluated after heart transplantation and/or VAD insertion in women. Fifty women who were status-post heart transplantation filled out a Herth Hope Index, Multiple Affect Adjective Checklist, and SF-12.¹² This study revealed that they had moderately low hope and relatively high anxiety, depression, and hostility. Hope was found to be an independent predictor of mood and quality of life. A certain patient of mine, who had redo sternotomy and heart transplantation a few years earlier, would say, "I'm in pretty good shape for the shape I'm in." A positive attitude works, but providing false hope is not a kindness to the patient or her family.

Interestingly, in a study on the change in the quality of life after LVAD implementation to after heart transplantation, only 1 patient was a woman (out of 40).¹³ Another review of lifestyle and quality of life in long-term survivors of cardiac transplant included only 8 women among 93 patients. The investigators did realize that their study findings could not be applied to women because of their underrepresentation.¹⁴

As health care providers, we ask a lot of our patients, regardless of gender. We ask them to take any number of medications; learn how to take care of a mechanical assist device; go through one, two, or several operations; and then take more medications. As we gain in experience with respect to heart transplantation and devices, questions regarding quality of life must be asked. Answers for women will lag behind until their representation is increased and the clinical database reflects their participation. In the future, women may receive more devices as destination therapy is more frequently applied in older patients and as devices are designed for use in smaller patients.

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