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Peripartum cardiomyopathy: Post-transplant outcomes from the united network for organ sharing database

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BACKGROUND: Nearly 25% of patients with peripartum cardiomyopathy (PPCM) will require cardiac transplantation. Whether post-transplant outcomes differ among patients with PPCM compared with other recipients remains unsettled.

METHODS: The United Network for Organ Sharing database was queried for cardiac transplants, comparing characteristics and outcomes for PPCM, other women, and all others.

RESULTS: Between 1987 and 2010, 42,406 patients (9,419 women and 32,987 men) received a heart transplant. Of these, 485 women who had PPCM as the indication were younger ($p < 0.001$), had higher sensitization ($p < 0.001$), required higher intensity of cardiovascular support pre-transplant ($p = 0.026$), and had higher listing status ($p < 0.001$). Those with PPCM had more post-transplant rejection during the index transplant hospitalization ($p < 0.001$) and during the first year ($p = 0.003$). Comparing PPCM with other women and all others, graft survival was inferior ($p = 0.004$ and $p < 0.003$, respectively) and age-adjusted survival was lower ($p < 0.001$ and $p = 0.02$, respectively).

CONCLUSIONS: This large report shows outcomes of graft failure and death are inferior for recipients with PPCM, which may be partly explained by younger age, higher allosensitization, higher pre-transplant acuity, and increased rejection. More research is needed to determine management strategies to improve outcomes in PPCM heart transplant recipients.

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Peripartum cardiomyopathy (PPCM) is defined as the occurrence of symptomatic left ventricular dysfunction manifested between the last month of pregnancy through the fifth postpartum month in otherwise healthy women.[1] Recent reports have suggested 6% to 23% of women with PPCM will require cardiac transplantation.[2,3] Predictors of death or need for cardiac transplantation in PPCM have included younger age, non-white race, delay in diagnosis, and lower left ventricular ejection fraction at the time of diagnosis.[4] PPCM is a relatively rare condition, and therefore, transplant in PPCM patients represents a low proportion of patients who receive a heart transplant. Therefore, experience with this cohort of transplant recipients is limited, and published literature consists mainly of small case reports and case series.[5–10]

Prior analyses have generally shown favorable post-transplant outcomes for women with PPCM who receive allografts; however, the numbers of patients studied have been small.[5–8] The most recent report from the Cardiac Transplant Research Database (CTRD) examined the post-transplant course in 80 patients with PPCM and suggested similar outcomes to other cardiac transplant recipients of a similar age.[5] The first CTRD analysis a decade earlier showed favorable outcomes of 40 patients with PPCM.[6] Two smaller reports of 10[7] and 8[8] patients with PPCM had excellent post-transplant outcomes, especially when compared with other recipients who received allografts for idiopathic dilated cardiomyopathy (IDCM). Concerns that

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women with PPCM may have poor post-transplant outcomes compared with other transplant recipients had thus far not been validated.[7,8] The purpose of this study was to attempt to settle the controversies regarding outcomes in PPCM cardiac transplant recipients through an analysis of the United Network for Organ Sharing (UNOS) database UNet.

Methods

This study was approved by the Intermountain Healthcare Institutional Review Board.

Patient population and data source

Standard Transplant Analysis and Research (STAR) files were acquired for analysis from the United Network for Organ Sharing (UNOS) registry between the years 1987 and 2010 and were based on Organ Procurement and Transplantation Network (OPTN) data as of May 20, 2010. The data set included all reported cardiac transplant recipients aged 18 years and older.

Patients with PPCM were compared with other female (OF) recipients as the primary comparison, with all other (AO) recipients being of secondary interest to assess for the possibility of sex-related and PPCM-related differences in outcomes. Pre-transplant baseline characteristics evaluated included age, waiting time, listing status while waiting for transplant, pre-transplant panel reactive antibody (PRA) level, hospitalization status at time of transplant, and level of pre-transplant cardiovascular support, including intra-aortic balloon pump (IABP), inotropes, left ventricular assist device (LVAD) and/or right ventricular assist device (RVAD). Pregnancy history for all women was also assessed. The PRA data were listed as the highest percentage of class I or class II, because of the method of PRA acquisition before 2004, when only 1 PRA was documented. The listing status included status 1A and "old" status 1 (highest acuity), 1B (next highest acuity), and status 2 (including more stable patients).

Post-transplant characteristics and outcomes

Post-transplant characteristics and outcomes included allograft rejection (acute episode from index transplant to discharge and acute rejection within 1 year after transplant), actuarial graft survival, time to graft failure, and causes of death. Other variables of interest include ischemic time and length of stay immediately after transplant. Causes of death were grouped into several main categories. Finally, actuarial graft survival for all 3 groups was assessed.

Because PPCM recipients were significantly younger and had different baseline characteristics and acuity than OF and AO recipients, multivariable Cox survival analyses were performed to correct for survival differences initially apparent between PPCM and the other groups but actually attributable to variables such as patient age, previous pregnancy, or PRA. Such multivariable modeling permitted the determination of whether the PPCM diagnosis or some other factor actually accounted for the observed survival differences. Graft survival was assessed by transplant era from 1987 to 1999 and from 2000 to May 2010.

Statistical analysis

Univariable analysis was performed using the Student *t*-test for continuous variables and the chi-square test for the categoric variables to determine differences between the PPCM and OF or AO groups. Univariable survival analyses used Kaplan-Meier methods and univariable Cox regression. A value of $p \leq 0.05$ was considered statistically significant. Cox regression was performed to determine the time to graft failure for PPCM recipients compared with OF and AO recipients, with multivariable Cox analyses adjusting for patient age in the full population.

Secondary multivariable models adjusted for other common clinical risk characteristics as well as age, but did so in reduced sample sizes because substantially less than all of the patients had data for the following variables: PRA, ischemic time, UNOS status, LVAD, IABP, intravenous (IV) inotropes, treated for rejection before discharge, treated for rejection within 1 year after transplant, and previous pregnancy in women.

Kaplan-Meier survival curves were constructed for the 3 groups to demonstrate post-transplant graft survival, defined as being alive at the cutoff date for our study without having needed retransplantation. Redo transplant was counted as a primary cardiac death end point, and all retransplant recipients were censored at this time point. Data were analyzed using SPSS 17.0 software, (SPSS Inc, a division of IBM, Chicago, IL) and are expressed as the mean ± standard deviation, unless otherwise specified.

Results

Pre-transplant baseline characteristics

Between October 1987 and May 2010, 42,406 cardiac transplant recipients were reported to OPTN, comprising 32,987 men (78%) and 9,419 women (22%). There were 485 women who had a pre-transplant diagnosis of PPCM, representing 1% of all transplants and 5% of transplants in women. PPCM was the fourth leading indication for transplant in women, following idiopathic cardiomyopathy (44.8%), ischemic dilated cardiomyopathy (17.1%), and coronary artery disease (9.5%). All UNOS regions have performed transplants for the indication of PPCM, ranging in experience from 13 to 77 patients.

The baseline characteristics of the 3 groups are listed in Table 1. PPCM patients were significantly younger, had higher PRA, higher number of previous pregnancies, longer waiting time, higher rates of hospitalization while awaiting transplant, and higher listing status.

Post-transplant outcomes

The PPCM group had a higher incidence of rejection compared with OF and AO recipients, both during the index transplant hospitalization and within the first year after transplant (Table 2). Graft survival was significantly shorter in PPCM recipients compared with OF and AO. PPCM recipients also had higher rates of retransplantation than OF and AO (Table 2). Graft ischemic time and index hospitalization length of stay were similar for all recipients. Fewer