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Mortality, rehospitalization, and post-transplant complications in gender-mismatched heart transplant recipients

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ABSTRACT

Background: Limited research has been published on outcomes in heart transplant (HT) recipients with gender-mismatched donors.
Objective: Compare 3-year post-transplant outcomes in 2 groups of gender-mismatched HT recipients and a no-mismatch group.
Methods: Sample: 347 HT recipients: 21.3% (74) received a heart from the opposite gender: Group 1: same gender donor/recipient (273, 78.7%); Group 2: female donor/male recipient (40, 11.5%); Group 3: male donor/female recipient (34, 9.8%). Outcomes: mortality, hospitalization, and complications.
Results: Female patients with male heart donors had shorter 3-year survival, were rehospitalized more days after HT discharge, and had more treated acute rejection episodes and cardiac allograft vasculopathy. No differences were found in: HT length of stay, respiratory failure, stroke, cancer, renal dysfunction, steroid-induced diabetes, number of IV-treated infections, or the timing of infection and rejection.
Conclusion: Female HT recipients with male donors had worse 3-year outcomes as compared to male-mismatch and no-mismatch groups.

Background

Limited research has been published on heart transplant (HT) outcomes in patients with gender-mismatched organ donors, and many of the findings differ on which type of gender-mismatch (if any) has a worse prognosis for post-transplant outcomes. In addition, most studies on HT gender-mismatch focused solely on patient survival, although a few articles reported differences in acute rejection, cardiac allograft vasculopathy (CAV), and graft survival.

Our 2012 research[1] on gender-mismatched HT recipients examined additional outcomes not previously reported in this population, but only for the first year after surgery. Our previous study showed that female-mismatch patients (male donor/female recipient) had more episodes of acute rejection and more rehospitalization after the HT discharge. However, no significant gender-mismatch differences were found in first-year death rates, survival time, length of stay for the HT admission, or the incidence of infection, CAV, renal dysfunction, steroid-induced diabetes, or cancer.

Abbreviations: BMI, body mass index; CAD, coronary artery disease; CAV, cardiac allograft vasculopathy; CMV, cytomegalovirus; EENT, eye, ear, nose, and throat; GI, gastrointestinal; HT, heart transplant; HTN, hypertension; IABP, intra-aortic balloon pump; ISHLT, International Society for Heart and Lung Transplantation; IV, intravenous; MI, myocardial infarction; NIH, National Institutes of Health; PE, pulmonary embolism; PRA, panel-reactive antibody; PVR, pulmonary vascular resistance; TAH, total artificial heart; UNOS, United Network for Organ Sharing; VAD, ventricular assist device.

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In other studies, variability in early and late mortality after HT surgery has been attributed to both male-mismatch and female-mismatch of heart donors and recipients, including registry data from the ISHLT (International Society for Heart and Lung Transplantation) and UNOS (United Network for Organ Sharing). Higher post-HT mortality has been reported in both types of gender-mismatch in 8 articles,[2–9] only in the female-mismatch patients (male donor/female recipient) in 1 article,[10] and only in the male-mismatch patients (female donor/male recipient) in 14 articles.[11–24] However, 2 studies found no difference in HT mortality due to gender-mismatch of either kind.[25,26]

In addition to our 2012 study,[1] several other studies have also found differences in HT rejection rates due to donor/recipient gender-mismatch. More rejection was reported only in the female-mismatch patients in 2 articles,[23,27] only in the male-mismatch patients in 1 article,[19] and in both types of gender-mismatch in 1 article.[28] However, 2 studies found no difference in HT rejection rates due to gender-mismatch.[15,26]

Fewer reports were found on CAV and graft failure in gender-mismatched HT recipients. An ISHLT report cited more CAV in male-mismatch patients,[16] whereas 2 other studies found no difference in CAV rates due to gender-mismatch.[4,15] In addition, more HT graft failure has been reported in both types of gender-mismatched patients in 2 articles[11,29] and only in male-mismatch patients in 2 articles.[30,31]

We could not identify any studies that reported HT length of stay or subsequent rehospitalizations in gender-mismatched HT patients, except for our previous research. Our 2008 study[32] found that female-mismatch was a significant predictor for the amount of time rehospitalized during the first year after HT surgery, and our 2012 study[1] found that female-mismatch patients were rehospitalized more days during the first year after the HT discharge. However, gender-mismatch of either kind did not affect the length of stay for the initial HT surgical admission in our earlier research.

Research objective

Because of the few types of outcomes examined in most of the previous HT studies on this topic and the mixed findings on which type of gender-mismatch portends worse outcomes after HT surgery, more research is needed to investigate the impact of gender-mismatch on a wider range of HT outcomes. Since our 2012 study[1] examined 10 post-transplant outcomes in gender-mismatched patients for only the first year after HT surgery, we extended the follow-up to 3 years in the same sample for this study and examined 15 outcomes. Therefore, the objective of this research was to compare 3-year post-transplant outcomes in 3 groups of HT recipients: 2 groups of gender-mismatched patients (male-mismatch and female-mismatch) and a group of no-mismatch patients. Outcomes examined pertained to mortality/survival, hospitalization (HT length of stay and subsequent rehospitalizations), and multiple post-transplant complications.

Methods

Source of data

The clinical data for this report came from our 10-year prospective, longitudinal NIH-funded study conducted at 2 U.S. hospitals. The study examined medical, physical, and psychosocial factors impacting on multiple HT outcomes both pre-operatively and post-transplant, using data collected from medical records and from patient-completed questionnaires pertaining to quality of life (e.g., symptoms, functional and work status, HT-related stressors, coping strategies, social support resources).[1,32–44] The study was approved by the Institutional Review Board at each hospital, and patients provided written informed consent.

Sample composition

The sample for this report consisted of 347 adult (18 or older) HT recipients (70 women, 20.2%, and 277 men, 79.8%) from 2 hospitals in the midwestern and southern United States, who were followed pre-operatively while they were on the HT waiting list and for 3 years after surgery. The percentage of women in this sample is similar to the ISHLT registry data.[7] Ages at transplant ranged from 20 to 71 years (mean = 52 ± 10, median = 54).

Seventy-four of the 347 patients (21.3%) received a heart from the opposite gender, which is similar to the average of 24% gender-mismatch in other HT studies. Three groups of patients were compared in our research: Group 1: no-mismatch: same gender donor and recipient (N = 273, 78.7%: 36 women and 237 men); Group 2: male-mismatch: female donor and male recipient (N = 40, 11.5%); and Group 3: female-mismatch: male donor and female recipient (N = 34, 9.8%).

Data

Clinical data covered the entire pre-transplant and post-transplant periods, and was collected every 3 months while patients waited for a HT, then 1, 3, 6, 9, and 12 months after surgery, and then every 6 months post-HT for years 2 and 3. Data obtained from inpatient and outpatient medical records included: pre-transplant patient characteristics, pre-operative and post-transplant medical and surgical history, mortality and causes of death, post-HT complications (e.g., rejection, infection, CAV), lab test results, medications, hospitalizations (dates, reasons), and donor characteristics. Several methods were used to assess the reliability of the retrieval, recording, coding, and computer entry of the clinical data, as described in our previous report.[32]

Sample size over time

Once patients went on the HT waiting list, they were recruited for this study while they were in the hospital or when they came to the clinic for follow-up. A total of 550 HT candidates were enrolled in the study from a pool of 696 adult HT candidates on the waiting list at the 2 hospitals (Fig. 1); therefore, 79% of the pool were able to be enrolled (reasons for non-enrollment are shown on Fig. 1).

However, 92 patients died while on the HT list, and 87 patients dropped out of the study for illness reasons while waiting for the HT. During our 10-year study, 347 patients received their HT, but 72 patients died during the first 3 years after surgery, and 5 patients dropped out of the study for work or health reasons during the 3-year post-transplant period (Fig. 1).

Therefore, by the time our 10-year study ended, data was available on 269 patients at 1 year after HT, on 215 patients at 2 years after HT, and on 145 patients at 3 years after HT (Fig. 1). The remainder of the patients had not yet reached those post-transplant time points when the funding expired, due to the long wait for a HT; mean wait was 276 days (median = 181 days; range = 3 days to 5+ years).

Outcomes

The following outcomes were compared in the 3 donor/recipient gender groups for the first 3 years after HT surgery: (1) mortality/survival: the incidence of death and length of survival; (2) hospitalization: hospital length of stay for the HT admission,