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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.

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Keywords

Heart transplant gender-mismatch; female-mismatched heart transplant outcomes; female-mismatched heart transplant survival; female-mismatched heart transplant rehospitalization; female-mismatched heart transplant rejection; female-mismatched cardiac allograft vasculopathy

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 research¹ 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.

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 study³² found that female-mismatch was a significant predictor for the amount of time rehospitalized during the first year after HT surgery, and our 2012 study¹ 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 study¹ 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 also examined more outcomes (15). 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 (Figure 1); therefore, 79% of the pool were able to be enrolled (reasons for non-enrollment are shown on Figure 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 (Figure 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 (Figure 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, number of times rehospitalized after the HT discharge, and total number of days rehospitalized; (3) rejection: number of episodes of treated acute rejection plus the length of time to the first treated rejection; (4) infection: number of episodes of infections treated with IV (intravenous) antibiotics plus the length of time to the first IV-treated infection; and (5) the incidence of post-transplant complications of respiratory failure, stroke, cardiac allograft vasculopathy, cancer (including skin cancer), new-onset steroid-induced diabetes, and severe renal dysfunction (defined as a serum creatinine >2.5 mg/dl or a diagnosis of renal failure or being on dialysis, using the ISHLT definition⁷).

Statistics

To increase the power of the study because of the relatively small number of patients in the 2 gender-mismatched groups (40 and 34), a more conservative probability level of $P = .025$ was used (instead of .05) to determine significant differences between groups. Pre-transplant baseline characteristics of the 3 groups were compared with logistic regression for categorical variables (using the paired comparisons contrasts procedure) and one-way analysis of variance (ANOVA) for continuous variables (using the Tukey paired comparisons test).

Kaplan-Meier analysis (with the paired comparisons procedure) was used to examine 3 continuous time-to-event outcomes: number of days survived during the first 3 years after surgery, number of days to the first treated rejection, and number of days to the first IV-treated infection. One-way ANOVA (with the Tukey test) was used to examine the rest of the continuous outcomes, and logistic regression (with the contrasts procedure) was used to examine the categorical outcomes.

RESULTS

Baseline Characteristics

Six of 23 baseline characteristics were significantly different between the donor/recipient gender groups (Table 1). Group 2 (male-mismatch: female donor/male recipient) had older donors, the highest pre-HT creatinine level, and the highest percentage of patients with CMV (cytomegalovirus) mismatch (donor positive/patient negative). Group 3 (female-mismatch: male donor/female recipient) was the youngest of the 3 groups, had the lowest percentage of patients with ischemic heart disease as the reason for HT, and had a much higher percentage of minority patients (3 times more than the other 2 groups: 38.2% vs 12.1% and 12.5%).

Post-Transplant Outcomes

Six outcomes were significantly different between the 3 donor/recipient gender groups during the first 3 years after HT surgery: incidence of death, length of survival, number of times and total number of days rehospitalized after the HT discharge, the number of acute rejections, and the incidence of CAV (Table 2). Nine outcomes were not significant: HT length of stay, number of days to the first treated acute rejection episode, number of IV-treated infections and number of days to the first IV-treated infection, and the incidence of respiratory failure, stroke, cancer, severe renal dysfunction, and steroid-induced diabetes (Table 2). The significant outcomes are described below.

Mortality/Survival

Seventy-two patients in the overall sample of 347 HT recipients died during the first 3 years after HT surgery (20.7%). A much higher percentage of Group 3 (male donor/female recipient) died during this post-transplant period (Table 2): 41.2% in Group 3 (female-mismatch) vs 17.9% in Group 1 (no-mismatch, $P = .002$) vs 22.5% in Group 2 (male-mismatch, $P = .023$).

Therefore, the mean length of time survived was also significantly shorter in Group 3 (Table 2): 795 days in Group 3 (female-mismatch) vs 928 days in Group 1 (no-mismatch, $P = .004$) vs 879 days in Group 2 (male-mismatch, $P = .025$). The Kaplan-Meier survival curves in Figure 2 depict the pronounced drop-off in survival beyond the first year after HT surgery in the female-mismatch patients as compared to the other 2 groups. Infection and acute rejection were the leading causes of death during the first 3 years after HT surgery in all 3 groups; other more frequent causes were stroke, MI, and CAV (Table 3).

Hospitalization

Length of stay for the HT surgical admission was not significantly different between the 3 donor/recipient gender groups (Table 2). However, rehospitalization after the HT discharge was significant: Group 3 (female-mismatch) was rehospitalized more times ($P = .001$) and more days ($P = .001$) than the other 2 groups during the first 3 years after the surgical discharge (Table 2). The most common reasons for re-admissions in Group 3 were: acute rejection, cardiovascular problems, infection, and pulmonary problems (Table 4).

Rejection

Group 3 (female-mismatch) had more episodes of treated acute rejection during the first 3 years after HT surgery than the other 2 groups: Group 3 vs Group 1 (no-mismatch): $P = .008$; Group 3 vs Group 2 (male-mismatch): $P = .021$ (Table 2).

Cardiac Allograft Vasculopathy

Group 3 also had a much higher incidence of CAV during the first 3 years after HT surgery than the other 2 groups (Table 2): 32.4% in Group 3 (female-mismatch) vs 12.1% in Group 1 (no-mismatch, $P = .002$) vs 12.5% in Group 2 (male-mismatch, $P = .009$).

DISCUSSION

In summary, female HT patients who received a heart from a male donor (Group 3) had 6 significantly worse outcomes during the 3-year period after HT surgery, as compared to male patients who received a female heart (Group 2) and patients who received a donor heart from the same gender (Group 1). These worse post-transplant outcomes in Group 3 (female-mismatch) were: a higher incidence of death and shorter 3-year survival, more times and more days rehospitalized after the HT discharge, more episodes of treated acute rejection, and a higher incidence of CAV.

Mortality/Survival

In our current study, female HT recipients with a male donor had significantly decreased survival on 3-year follow-up, which is in contrast to our previous 2012 research¹ that did not find any significant mortality difference in the female-mismatch patients in this same sample on shorter 1-year follow-up. The 3-year Kaplan-Meier survival curves reported in Figure 2 clearly depicted the drop-off in survival after the first post-transplant year in the female-mismatch patients as compared to both the male-mismatch and no-mismatch groups, and therefore identifies the reason for the mortality difference in our previous 1-year findings and the current 3-year findings.

Based on documentation in medical records, the most frequent causes of death in the female-mismatch patients during the first 3 years after surgery were acute rejection and infection, which are well-recognized mortality causes in all HT patients in general based on data from the ISHLT.^{2,5-7,11,13,16} In addition, as compared to the no-mismatch group, the female-mismatch patients had a higher proportion of deaths due to cardiopulmonary causes such as MI, CAV, PE, and respiratory failure. However, it should be kept in mind that the raw numbers were very small, since the total number of deaths in the female-mismatch patients was only 14 (but 41.2% of the group).

In agreement with our results, most of the previous HT research (including ISHLT and UNOS data) showed that gender-mismatch had a detrimental impact on survival on both short-term and long-term follow-up,²⁻²⁴ with most of the studies (14) reporting higher mortality only in the male HT recipients with a female donor. Worse survival in the male-mismatch patients is usually attributed to weight-mismatch or size-mismatch, in which the heart from a smaller female donor cannot meet the cardiac demands of the larger male recipient.^{18,24} However, only 1 study reported worse survival in the female-mismatch HT patients but not in the male-mismatch patients,¹⁰ as our study found.

Hospitalization

Although we found no difference in the length of stay for the HT admission between the 3 donor/recipient gender groups, our study demonstrated that gender-mismatched patients in Group 3 (male donor/female recipient) were rehospitalized a significantly greater number of times and also total number of days for the first 3 years after the surgical discharge. Re-admissions in the female-mismatch patients were most commonly due to acute rejection, infection, and cardiopulmonary problems. No other studies were identified on rehospitalization after the HT discharge in gender-mismatched HT recipients, except for our 2012 report in which female-mismatch patients also had significantly more rehospitalization for the first year after HT.¹

Rejection and CAV

In our current study, female-mismatch patients (male donor/female recipient) also had significantly more episodes of treated acute rejection during the first 3 years after HT surgery than either the male-mismatch or no-mismatch groups, a finding that is supported by 3 other studies.^{1,23,27} However, divergent results on HT rejection due to gender-mismatch have also been reported, with some studies finding more rejection only in the male-mismatch patients or in both types of gender-mismatch,^{19,28} and other studies finding no difference in rejection rates due to gender-mismatch of either kind.^{15,26}

Research has shown that more rejections are a risk factor for the development of CAV,^{6,16} and our present study did find a higher incidence of CAV during the first 3 years after HT surgery in the female-mismatch patients (the same group with more rejections). However, in contrast to our CAV result, divergent results have also been reported on CAV due to gender-mismatch, with ISHLT data finding more CAV only in male-mismatch patients,¹⁶ and other studies finding no difference in CAV rates due to gender-mismatch of either kind.^{4,15}

Prendergast²³ and Keogh²⁷ also found more rejections in gender-mismatched HT patients with a male donor and a female recipient, as our study did. To explain the propensity for rejection in HT females, Lietz⁴⁵ points out that female patients have a heightened immune response to antigens in transplanted organs, which predisposes them to more rejection. Reasons cited for this increased alloreactivity in females are: a differential effect of the sex hormones on the immune system, more autoimmune diseases in women, sensitization due to prior pregnancy, and the younger age of female HT recipients (as in our study) due to the increased immune responsiveness with younger age.^{18,27,46–50}

Moreover, Lietz⁴⁵ notes that this heightened immune response in female transplants is even more evident when a woman receives a man's heart, as found in our present study on 3-year post-transplant follow-up. In further support of this gender-mismatch effect on female organ rejection, our 2012 article¹ (with this same sample) also reported a higher rate of acute rejection on short-term follow-up for the first year after HT in women with a male donor. Therefore, Keogh²⁷ notes that female HT recipients with a male donor may require higher doses of steroids to offset this propensity for more rejections.

Possible Minority Effect

In our current study, more than a third (38.2%) of the female-mismatch patients were minorities (mainly African-American), as compared to only 12.1% and 12.5% of the other 2 groups. Previous research has reported worse HT outcomes in minority patients in many areas: shorter survival, more rejection and infection, more hospitalizations and rejection-related hospital stays and deaths, and a higher rate of CAV and steroid-induced diabetes.^{51–60} Therefore, the question arises whether the poorer HT outcomes in the female-mismatch patients in our study could partly be due to the larger proportion of minorities in this group, in addition to the effects of receiving a gender-mismatched heart, and being female and younger. However, we did not control for race in the analysis because there were only 51 minorities in the entire sample, so the number of minorities in the 2 gender-mismatched groups was very small (5 and 13), and the results would not have been trustworthy. Therefore, this is an area in need of investigation in future gender-mismatched HT studies with larger minority samples.

Conclusions

Female-mismatched HT recipients with male donors incurred more deaths and experienced shorter survival during the first 3 years after HT surgery, were rehospitalized more times and more days after the HT discharge, and had more post-transplant complications due to acute rejection and CAV, as compared to either male-mismatched patients or non-mismatched patients.

Study Limitation and Strengths

The main limitation of this research is that the gender-mismatched patients accounted for only 21.3% of the sample (74 patients), which may have decreased the ability to detect significant differences in some of the outcomes. However, strengths of this research are: (1) a more conservative probability level of .025 (rather than .05) was used to increase the

power of the study so that only meaningful results were considered significant in the smaller sample; (2) longitudinal analyses were conducted on multiple HT outcomes in patients at 2 hospitals in different geographic regions of the United States; and (3) comprehensive clinical data was collected at frequent intervals both pre-operatively and post-operatively, which spanned the entire pre-transplant wait and the post-transplant follow-up for 3 years after surgery.

Study Implications

Due to the shorter survival and the higher incidence of complications in the female-mismatched HT recipients with male donors, this group may need close monitoring by physicians and nurses for post-transplant problems. In addition, our rehospitalization findings provide new information on the greater use of hospital resources for the first 3 years after transplant surgery by gender-mismatched female HT patients who received a heart from a male donor, which also indicates higher costs for the post-transplant care of female-mismatched HT recipients. However, because of the relatively small number of gender-mismatched patients in our sample, the findings of this study need to be replicated with a larger number of gender-mismatched HT recipients.

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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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Figure 1.
Flow chart depicting the evolution of the heart transplant (HT) sample from enrollment in the study to 3 years after surgery.

Figure 2.

Kaplan-Meier survival curves for the first 3 years after heart transplant surgery by donor/recipient gender group (N = 347), indicating shorter survival in Group 3 (female-mismatch: male donor/female recipient). Mean number of days survived: Group 1 (no-mismatch): 928 ± 22 days; Group 2 (male-mismatch): 879 ± 67 days; Group 3 (female-mismatch): 795 ± 69 days. Log rank tests significant: Group 3 (female-mismatch) vs Group 1 (no-mismatch): P = .004; Group 3 (female-mismatch) vs Group 2 (male-mismatch): P = .025.

Table 1Baseline Characteristics of 347 HT Patients by Donor/Recipient Gender Group^a

Characteristic	Group 1 (N = 273)	Group 2 (N = 40)	Group 3 (N = 34)	P ^b
Patient age at HT (years)	§53 ± 10	‡53 ± 11	§‡48 ± 12	§.018 ‡.023
Donor age (years)	26 ± 9	‡32 ± 12	‡24 ± 9	‡.000
Minority race ^c	§12.1%	‡12.5%	§‡38.2%	§.000 ‡.001
Urgent priority for HT	48.4%	50.0%	44.1%	.869
Re-transplant	5.1%	2.5%	0	.319
CAD as reason for HT ^d	§54.9%	‡62.5%	§‡26.5%	‡.003 §.005
IV inotropes at HT	56.4%	55.0%	61.8%	.814
VAD or TAH at HT	9.2%	10.0%	5.9%	.794
IABP at HT	8.1%	7.5%	2.9%	.565
Ventilator at HT	4.8%	0	0	.160
Days on mechanical support	6 ± 23	15 ± 47	3 ± 9	.101
Time on HT list (days)	291 ± 293	222 ± 218	213 ± 216	.129
Ischemic time (minutes)	181 ± 58	182 ± 58	169 ± 60	.511
Pre-HT diabetes	18.3%	22.5%	17.6%	.806
Pre-HT COPD	10.5%	20.0%	14.7%	.320
History of smoking	67.4%	65.0%	61.8%	.786
Pre-HT creatinine (mg/dl)	§1.4 ± 0.5	‡1.5 ± 0.4	§‡1.1 ± 0.3	‡.001 §.005
Pre-HT cholesterol (mg/dl)	182 ± 47	178 ± 43	178 ± 51	.809
Pre-HT PRA >10%	8.1%	10.0%	8.8%	.913
Pre-HT PVR (Wood units)	2.4 ± 1.4	2.2 ± 1.1	2.5 ± 1.3	.548
Patient BMI (kg/m ²) at HT	26 ± 4	24 ± 4	24 ± 4	.035
Weight mismatch ^e	28.2%	32.5%	41.2%	.278
CMV mismatch ^f	11.4%	‡27.5%	‡5.9%	‡.007

Abbreviations: BMI, body mass index; CAD, coronary artery disease; CMV, cytomegalovirus; COPD, chronic obstructive pulmonary disease; HT, heart transplant; IABP, intra-aortic balloon pump; IV, intravenous; PRA, panel-reactive antibody; PVR, pulmonary vascular resistance; TAH, total artificial heart; VAD, ventricular assist device.

^aGroup 1: no-mismatch: same gender donor/recipient (78.7%); Group 2: male-mismatch: female donor/male recipient (11.5%); Group 3: female-mismatch: male donor/female recipient (9.8%).

^bSignificance determined at P .025; Note: groups with the same superscript symbol (either § or ‡) are significantly different on that variable: symbol § compares Group 1 vs Group 3; symbol ‡ compares Group 2 vs Group 3.

^cMinorities included: African-Americans, Hispanics, and Asians.

^dOther reasons for HT included: cardiomyopathy, valvular heart disease, congenital heart disease, myocarditis, and previous graft failure.

^eWeight mismatch: >20% difference between patient weight and donor weight in kilograms.

^fCMV mismatch: donor positive/patient negative.

Table 23-Year Post-Transplant Outcomes in 347 Heart Transplant Patients by Donor/Recipient Gender Group^a

Outcome	Group 1 (N = 273)	Group 2 (N = 40)	Group 3 (N = 34)	P ^b
Died	§17.9%	‡22.5%	§‡41.2%	§.002 ‡.023
Length of survival (days)	§928 ± 22	‡879 ± 67	§‡795 ± 69	§.004 ‡.025
HT length of stay (days)	20 ± 18	23 ± 14	18 ± 9	.571
Times rehospitalized	§6 ± 5	‡5 ± 5	§‡9 ± 10	‡.001 §.001
Days rehospitalized	§32 ± 37	‡23 ± 26	§‡56 ± 55	‡.001 §.001
Number of treated acute rejections	§3 ± 3	‡3 ± 4	§‡5 ± 4	§.008 ‡.021
Days to first treated rejection	176 ± 21	161 ± 52	139 ± 54	.139
Number of IV-treated infections	2 ± 3	2 ± 3	2 ± 3	.984
Days to first IV-treated infection	429 ± 29	337 ± 75	431 ± 82	.298
Respiratory failure	22.0%	20.0%	32.4%	.366
Stroke	7.7%	2.5%	5.9%	.389
CAV	§12.1%	‡12.5%	§‡32.4%	§.002 ‡.009
Cancer ^c	13.6%	17.5%	8.8%	.543
Severe renal dysfunction ^d	14.7%	25.0%	5.9%	.064
Steroid-induced diabetes	14.7%	17.5%	17.6%	.826

Abbreviations: CAV, cardiac allograft vasculopathy; HT, heart transplant; IV, intravenous.

^aGroup 1: no-mismatch: same gender donor/recipient (78.7%); Group 2: male-mismatch: female donor/male recipient (11.5%); Group 3: female-mismatch: male donor/female recipient (9.8%).^bSignificance determined at P .025; Note: groups with the same superscript symbol (either § or ‡) are significantly different on that variable: symbol § compares Group 1 vs Group 3; symbol ‡ compares Group 2 vs Group 3.^cCancers included: lymphoma, liver cancer, kidney cancer, and non-melanoma skin cancer.^dDefined as a serum creatinine >2.5 mg/dl or a diagnosis of renal failure or on dialysis.⁷

Table 3

Causes of 72 Deaths in 347 Heart Transplant Patients (20.7%) During the First 3 Years After Surgery by Donor/Recipient Gender Group^a

Cause of Death ^b	Group 1 (N = 273) # (%)	Group 2 (N = 40) # (%)	Group 3 (N = 34) # (%)	Total Deaths
Infection	18 (36.7%)	2 (22.2%)	3 (21.4%)	23
Acute rejection	6 (12.2%)	3 (33.3%)	4 (28.6%)	13
Stroke	7 (14.3%)	0	0	7
MI	3 (6.1%)	0	1 (7.1%)	4
CAV	2 (4.1%)	1 (11.1%)	1 (7.1%)	4
Right ventricular failure	2 (4.1%)	1 (11.1%)	0	3
Multi-organ failure	2 (4.1%)	1 (11.1%)	0	3
Intra-operative pump failure	2 (4.1%)	0	1 (7.1%)	3
Lymphoma	3 (6.1%)	0	0	3
Pulmonary embolism	1 (2.0%)	0	1 (7.1%)	2
Respiratory failure	0	1 (11.1%)	1 (7.1%)	2
Pancreatitis	2 (4.1%)	0	0	2
Late graft failure	0	0	1 (7.1%)	1
Aortic aneurysm	0	0	1 (7.1%)	1
Intra-operative hemorrhage	1 (2.0%)	0	0	1
Number of deaths	49	9	14	72
% of each group who died	17.9%	22.5%	41.2%	

Abbreviations: CAV, cardiac allograft vasculopathy; MI, myocardial infarction.

^a Group 1: no-mismatch: same gender donor/recipient (78.7%); Group 2: male-mismatch: female donor/male recipient (11.5%); Group 3: female-mismatch: male donor/female recipient (9.8%).

^b Source of cause of death data: autopsy report (36) or death certificate (16) or physician note on the chart (20).

Table 4

Discharge Diagnoses for Hospital Re-admissions During the First 3 Years After Heart Transplant Discharge in 347 Patients by Donor/Recipient Gender Group^a

Discharge Diagnosis	Group 1 (N = 273) % of Diagnoses	Group 2 (N = 40) % of Diagnoses	Group 3 (N = 34) % of Diagnoses
Acute rejection	35.8	37.9	37.4
Infection	17.4	16.9	11.7
Cardiovascular (e.g., CAV, MI, arrhythmias, pericarditis, mitral regurgitation, cardiac tamponade)	10.3	9.2	19.6
Pulmonary (e.g., pneumonia, pulmonary edema, pulmonary embolism, respiratory failure)	8.7	7.2	9.8
Gastrointestinal (e.g., gastritis, pancreatitis, hepatitis, liver failure)	9.8	7.8	5.6
Renal (e.g., chronic renal insufficiency, renal failure, kidney stones)	3.8	2.6	2.3
Neurologic (e.g., stroke, encephalitis, seizures)	3.1	3.3	4.9
Orthopedic (e.g., avascular necrosis of hip, spinal fracture)	2.1	3.9	3.0
Endocrine (e.g., diabetes, hypothyroidism)	2.6	3.3	0.8
Oncologic (e.g., lymphoma, liver cancer, kidney cancer, skin cancer)	1.2	0	1.5
Hematologic (e.g., leukopenia, thrombocytopenia)	2.3	4.6	0.4
Miscellaneous diagnoses (e.g., EENT, urologic, dermatologic)	2.9	3.3	3.0

Abbreviations: CAV, cardiac allograft vasculopathy; EENT, eye, ear, nose and throat; MI, myocardial infarction.

^aGroup 1: no-mismatch: same gender donor/recipient (78.7%); Group 2: male-mismatch: female donor/male recipient (11.5%); Group 3: female-mismatch: male donor/female recipient (9.8%).