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First-Year Clinical Outcomes in Gender-Mismatched Heart Transplant Recipients

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Abstract

Background—Research indicates that gender mismatch of organ donor and recipient may adversely affect outcomes in heart transplant (HT) patients. However, there is a paucity of literature on gender-mismatched outcomes in patients receiving a HT, and only a few outcomes have been investigated.

Objectives—Objectives were to: (1) determine if gender-mismatched HT recipients experienced decreased survival, more post-transplant complications, and more days hospitalized during the first post-operative year as compared to gender-matched recipients; and (2) identify risk factors for decreased survival.

Methods—Patients were 347 HT recipients; 21.3% (74) received a heart from the opposite gender. Three groups were compared: Group 1: same gender donor-recipient (273, 78.7%: 36 women, 237 men); Group 2: female donor-male recipient (40, 11.5%); Group 3: male donor-female recipient (34, 9.8%). Ten outcomes were compared with Kaplan-Meier survival analysis, logistic regression, and MANCOVA, using a Bonferroni-adjusted $P = .005$. Risk factors for decreased survival were examined with Cox regression.

Results—Gender-mismatched HT patients with a male donor and a female recipient (Group 3) had more treated acute rejections and were rehospitalized more days after HT discharge during the first post-operative year as compared to gender-matched patients. No significant differences were found in 8 other first-year outcomes: number of deaths, survival time, hospital length of stay for HT surgery, cardiac allograft vasculopathy, severe renal dysfunction, new-onset steroid-induced diabetes, non-skin cancers, or the number of infections treated with an intravenous (IV) antibiotic. Risk factors for decreased year 1 survival were higher year 1 cholesterol, earlier IV-treated infection, severe renal dysfunction, earlier treated rejection, and diabetes (both pre-existing and new-onset steroid-induced diabetes).

Conclusion—Gender-mismatched HT recipients had more complications due to rejection and higher resource utilization due to more rehospitalization during the first post-operative year as

compared to gender-matched recipients. Therefore, these problem areas may provide targets for possible interventions.

Keywords

donor-recipient gender mismatch; heart transplant outcomes

Some studies have shown that gender mismatch of organ donor and recipient leads to adverse outcomes in heart transplant (HT) patients,^{1-14, 19, 20} although other studies found no difference in outcomes.^{15-18, 21} However, there is a paucity of literature on outcomes in gender-mismatched patients receiving a HT, and only a few outcomes have been investigated. Most of the studies on this topic examined patient survival, and a few studies examined acute rejection, infection, cardiac allograft vasculopathy (CAV), or graft survival.

Differences in various HT outcomes have been found with both types of gender mismatch (Table 1). Many of the studies reported higher mortality when the heart donor was female and the recipient male,^{1-7, 9-12, 14, 20} possibly due to weight mismatch or size mismatch (body surface area ratio) in which the heart from a smaller female donor could not meet the cardiac demands of the larger male patient.^{3, 20} A greater number of episodes of severe acute rejection⁴ and worse graft survival^{8, 12, 19} due to CAV have also been found with female donor-male recipient mismatch. In addition, higher mortality^{2, 3, 9, 11} and more rejection episodes^{10, 13} have also been reported with the opposite mismatch: when the donor was male and the recipient female. Registry data from the International Society for Heart and Lung Transplantation (ISHLT) show that gender mismatch is a risk factor for both short-term and long-term mortality in HT recipients.^{2, 22}

Objectives

Because of the limited types of outcomes examined in previous HT studies, more research is needed to investigate the impact of gender mismatch on additional outcomes in HT patients. Therefore, the objectives of this study were to: (1) determine if gender-mismatched HT recipients experienced worse clinical outcomes of decreased survival, more post-transplant complications, and a greater number of days hospitalized (either during or after the surgical admission) during the first post-operative year as compared to gender-matched recipients; and (2) identify risk factors for decreased survival (such as rejection, infection, and co-morbidities). We assessed outcomes during the first year after surgery because HT mortality during this period is higher than the next 4 years combined, according to the ISHLT registry report.²

Methods

Patients

The patients for this report were 347 adult HT recipients (70 women, 20.2%, and 277 men, 79.8%) from 2 medical centers: Loyola University of Chicago and University of Alabama at Birmingham. The percentage of women in this sample is similar to the ISHLT registry data.² Ages at transplant ranged from 20 to 71 years (mean = 52 ± 10, median = 54). This sample was from a pool of 696 adult (18) HT candidates at the 2 sites (Figure 1).

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 reporting on outcomes. Three groups of patients were compared in this study: **Group 1:** same gender donor and recipient (N = 273, 78.7%: 36 women and 237 men); **Group 2:** female donor and male

recipient mismatch (N = 40, 11.5%); and **Group 3:** male donor and female recipient mismatch (N = 34, 9.8%).

Procedure

Patients were enrolled in the study while awaiting HT and were followed for up to 5 years after surgery. Both medical data and patient-completed questionnaire data were collected at standardized intervals during the study by nurses experienced in cardiac care, as reported previously by Grady et al.²³ and Jalowiec et al.²⁴ Pre-operative data were collected every 3 months while patients were on the HT waiting list and first-year post-operative data were collected at 1, 3, 6, 9, and 12 months after transplant. The medical data collection covered the entire time both pre- and post-HT. Patients gave written informed consent to participate in this study. The research was approved by the Institutional Review Board at each site.

Outcomes

For this report, differences in 10 first-year outcomes were examined in the 3 donor-recipient gender groups: **(1) mortality/survival:** the incidence of death and length of survival; **(2) post-transplant complications:** the number of treated acute rejections (based on established ISHLT criteria), the number of IV-treated infections (infections treated with an intravenous antibiotic), the incidence of CAV, new-onset steroid-induced diabetes, non-skin cancers, and severe renal dysfunction (which was defined as a serum creatinine >2.5 mg/dl, a diagnosis of renal failure, or being on dialysis, using the definition of the ISHLT registry report²); and **(3) hospitalization:** hospital length of stay for the HT surgery and the number of days rehospitalized after discharge.

Data

Pre-operative and post-operative clinical data collected included medical and surgical history, intra-operative and post-operative complications, hospitalizations at the transplant site (dates and diagnoses), medications and treatments (immunosuppressant and non-immunosuppressant), laboratory results, and donor data.²⁴ Several methods were used to assess the reliability of the chart review data (of retrieval, recording, coding, computer entry), as described previously by Jalowiec et al.²⁴ The main method was a comparison of the original chart data to a sample of 25% of the study data, systematically chosen so that the data on many of the patients would be verified for some of the pre-operative and post-operative time periods.²⁴

Statistics

Data were analyzed with SPSS. Baseline characteristics of the 3 groups were compared with either: (1) Pearson chi square for 3×2 nominal contingency tables with examination of standardized residuals (if >2) to determine which group(s) influenced the statistic; or (2) ANOVA (analysis of variance) for continuous variables with the Tukey post-hoc test to identify which group comparisons were significant ($P < .05$).

Because of the multiple outcomes and multiple risk factors examined, a Bonferroni-adjusted $P < .005$ was used to determine significant group differences in outcomes and mortality risk factors. For objective #1 (outcomes), logistic regression was used to identify significant differences among the 3 groups in the incidence of 5 dichotomous outcomes during the first post-transplant year: deaths, severe renal dysfunction, new-onset steroid-induced diabetes, CAV, and non-skin cancers (using contrasts with Group 1 [no gender mismatch] as the reference group and covariates of patient age at HT and donor age).

For objective #1 (outcomes), MANCOVA (multivariate analysis of covariance) was used to identify significant group differences in 4 continuous outcomes: HT length of stay, number of days rehospitalized after the surgical discharge, number of treated rejections, and number of IV-treated infections (using contrasts with Group 1 as the reference group and covariates of patient HT age and donor age).

For objective #1 (outcomes), Kaplan-Meier time-to-event analysis (with pairwise comparisons and the log rank significance test) was used to calculate and compare survival curves for each donor-recipient gender group during the first post-operative year. For objective #2 (risk factors), Cox regression was used to identify risk factors for decreased survival. Univariate Cox regression was first used to identify potential individual covariates, which were then combined and tested in a multivariate Cox model to determine significant risk factors for decreased survival (using backward stepwise elimination and contrasts with Group 1 as the reference group).

For both Kaplan-Meier and Cox analyses, the dependent time variable for length of survival for censored cases (those who did not die within the first year and those who did not finish the first-year follow-up for reasons other than death) was the number of days of study follow-up during the first post-operative year. For Cox regression, variables that failed the crucial assumption of proportional hazards across time were converted to time-dependent covariates by creating an interaction term with time.

Results

Baseline Characteristics

Significant differences in the baseline characteristics (pre-operative and peri-operative) of the 3 donor-recipient gender groups were: (1) Group 2 (female donor-male recipient) had older donors and more patients with CMV (cytomegalovirus) mismatch (donor positive/patient negative); and (2) Group 3 (male donor-female recipient) was younger, had more minority patients, had fewer patients with pre-HT coronary artery disease (as opposed to non-ischemic heart disease), weighed less pre-HT (based on body mass index), and had lower serum creatinine at HT (Table 2).

Mortality/Survival Outcomes

Fifty-two of the 347 patients (15.0%) died during the first post-HT year; 38.5% of the deaths (20/52) occurred within the first month. Both gender-mismatched groups (2 and 3) had a higher percentage of deaths than Group 1 (no mismatch) but this difference was not significant (adjusted for patient age at HT and donor age) (Table 3). Infection and acute rejection were the leading causes of death during year 1 (Table 4).

For the overall sample (N = 347), the length of first-year survival ranged from 0 days (4 intra-operative deaths) to 365 days (mean = 307 ± 114 , median = 343). Although Group 2 (female donor-male recipient mismatch) showed worse survival than the other 2 groups both at 30 days and at 1 year, survival was not significantly different among the 3 groups (Figure 2).

Mortality Risk Factors

Significant risk factors for decreased year 1 survival were: higher year 1 cholesterol (Group 3: male donor-female recipient), earlier IV-treated infection (Group 2: female donor-male recipient), severe renal dysfunction (Group 2: female donor-male recipient), earlier treated rejection (Group 3: male donor-female recipient), and diabetes (both pre-existing and new-onset steroid-induced diabetes, Group 2: female donor-male recipient) (Table 5).

Post-Transplant Complications Outcomes

The number of treated acute rejections during year 1 ($N = 347$) ranged from 0 (19.6% of the patients) to 15 (mean = 3.0 ± 2.8). This was significantly different among the groups (adjusted for patient HT age and donor age): Group 3 (male donor-female recipient mismatch) had more treated rejections than the other 2 groups (Table 3). The number of IV-treated infections during the first year ($N = 347$) ranged from 0 (44.1% of the patients) to 14 (mean = 1.5 ± 2.4), which was not significantly different among the groups (adjusted for patient HT age and donor age) (Table 3). Also, there were no significant group differences ($N = 347$) in the first-year incidence of severe renal dysfunction (not significant at the Bonferroni-adjusted $P = .005$ but $P = .014$; Group 2 mismatch had more cases), new-onset steroid-induced diabetes, CAV, or non-skin cancers (adjusted for patient HT age and donor age) (Table 3).

Hospitalization Outcomes

For those who were discharged after transplant ($N = 320$, 92.2%; 27 patients died during the surgical admission), the hospital length of stay for HT surgery ranged from 5 days to 169 days (mean = 20 ± 17 , median = 17), and 13.1% (42/320) were hospitalized for more than a month after surgery. Length of HT hospital stay was not significantly different among the 3 groups (adjusted for patient HT age and donor age) (Table 3).

After discharge from the HT surgery, 88.4% of the patients (283/320) were readmitted during the first post-operative year, and of those rehospitalized, 39.6% (112/283) were readmitted within the first month. The most common reasons for first-year readmissions were acute rejection, infection, cardiac complications, and gastro-intestinal or hepatic problems.

The number of days rehospitalized after the HT discharge during the first year ranged from 0 days (11.6% of the patients) to 141 days (mean = 24 ± 26 , median = 15), which was significantly different among the groups (adjusted for patient HT age and donor age). Group 3 (male donor-female recipient mismatch) spent more days rehospitalized after the surgical discharge during year 1 than the other 2 groups (Table 3).

Discussion

Outcomes

Two outcomes were significantly worse for gender-mismatched HT patients: Group 3 (male donor-female recipient) had more treated acute rejections and was rehospitalized more days during the first post-operative year than the other 2 groups (using a Bonferroni-adjusted $P = .005$). However, there were no significant group differences in 8 other first-year outcomes: number of deaths or length of survival, hospital length of stay for the HT surgery, number of IV-treated infections, or the incidence of severe renal dysfunction, new-onset steroid-induced diabetes, CAV, or non-skin cancers.

Because only 2 of the 10 outcomes were significant in this sample of HT patients, it would seem that gender mismatch of heart donor and recipient need not be a relevant issue when selecting donors, although the significant differences were in important outcomes (treated rejections and time rehospitalized). However, outcomes beyond the first year were not examined in this report so the impact of gender mismatch on later outcomes in this sample is not known.

Contrary to our nonsignificant result on survival in gender-mismatched patients, most of the studies reported that gender mismatch had a detrimental impact on HT survival. However,

similar to our findings, 4 other research groups also found no significant difference in HT survival due to gender mismatch.^{15-17, 21} Several possible reasons could explain our lack of a significant difference in the length of HT survival due to gender mismatch: (1) the important mortality risk of weight mismatch >20% was not a significant risk factor for decreased survival in the Cox regression model; (2) this report included only the first post-transplant year; (3) there were not enough gender-mismatched patients to detect a significant difference in survival; or (4) no difference in survival due to gender mismatch existed in this sample. In addition, our nonsignificant results on some of the other outcomes may have been due to only a small number of cases with that complication within the first year (such as CAV and cancer).

However, our study did demonstrate that gender-mismatched patients in Group 3 (male donor-female recipient) were rehospitalized a significantly greater number of days after the surgical discharge during the remainder of year 1, so these patients may need closer monitoring for complications. None of the studies on gender-mismatched HT outcomes reported the number of days rehospitalized after HT discharge so this finding provides new information.

In this study, Group 3 (male donor-female recipient mismatch) also had significantly more treated acute rejections during the first post-transplant year, which may partially explain why they were rehospitalized for more days. In addition, Group 3 experienced their first treated rejection earlier after the transplant. Keogh et al¹³ and Prendergast et al¹⁰ also found more rejections in gender-mismatched HT patients with a male donor and a female recipient.

Several reasons have been postulated to explain the higher rate of rejection in female recipients with a male donor: different hormonal profiles, gender differences in antigens, pre-sensitization in previously pregnant women, more auto-immune diseases in women, female HT recipients being younger than male recipients (as in this study) and increased immune responsiveness with younger age.^{3, 13, 26-30} Therefore, female HT patients with a male donor may require higher doses of steroids to offset this propensity for more rejections.¹³

ISHLT registry data demonstrate that gender mismatch impacts HT survival, especially after the first year. These data showed that, although gender mismatch was a significant risk factor for first-year mortality only in patients older than 60 years (male donor-female recipient mismatch), it was significant for all ages at 5 years (female donor-male recipient mismatch), 10 years (both types of mismatch), and 15 years (both types of mismatch).^{2, 22} Other studies also reported decreased patient survival,^{1, 3-7, 9-12, 14, 20} more acute rejection episodes,^{4, 10, 13} and decreased graft survival^{8, 12, 19} due to CAV in gender-mismatched HT recipients. Therefore, even though gender matching does not occur in HT organ allocation, tailoring post-operative care based on the documented impact of gender mismatch on various HT outcomes may be reasonable.

Mortality Risk Factors

Because of the wide range in first-year survival times (0 days to 365 days), risk factors for decreased survival were examined. Significant dichotomous risk factors were severe renal dysfunction (most likely due to calcineurin-inhibitor immunosuppressants³¹⁻³³) and diabetes (pre-existing and steroid-induced); both risk factors were greater in Group 2 (female donor-male recipient mismatch). ISHLT registry data² and other research^{16, 34, 35} have identified pre-existing diabetes as a risk factor for both short-term and long-term mortality after HT. In addition, HT recipients are at even greater risk for developing new-onset diabetes and its complications because of post-transplant steroid therapy.³⁶⁻³⁸

Significant continuous risk factors for decreased survival were: higher year 1 cholesterol (Group 3: male donor-female recipient), earlier IV-treated infection (Group 2: female donor-male recipient), and earlier treated rejection (Group 3: male donor-female recipient). Higher post-transplant cholesterol conveyed the greatest risk for decreased first-year survival in this HT sample (based on the Wald statistic from Cox regression) and also has been identified as a risk factor for death in other HT studies.^{16, 39} In addition, hyperlipidemia is a well documented risk factor for developing post-transplant CAV, which can eventually lead to graft failure and death.⁴⁰⁻⁴⁴ In this sample, Group 3 (male donor-female recipient mismatch) who had significantly higher cholesterol also had the highest percentage of CAV, although this was not significant, probably due to the small number of cases in year 1 because CAV often takes longer to develop. Therefore, HT recipients with any of these 5 mortality risk factors (renal dysfunction, diabetes, elevated cholesterol, early infection, early rejection) will need aggressive treatment for these conditions to reduce the incidence of early death.

Limitations

Limitations of this research include: (1) only short-term outcomes were examined; (2) gender-mismatched patients accounted for only 21.3% of the sample, which may have decreased the power to detect significant differences in some of the outcomes; and (3) 2 of the 10 post-transplant outcomes (CAV and cancer) have a higher incidence later after HT and thus may not have been fully captured by this first-year analysis. Therefore, this study needs to be replicated with a larger number of gender-mismatched HT recipients, and post-operative data needs to be examined for longer than 1 year.

Conclusion

Gender-mismatched HT patients with a male donor and a female recipient had more complications due to rejection and higher resource utilization due to more rehospitalization during the first post-operative year as compared to gender-matched HT patients. Therefore, these problem areas may provide targets for possible interventions. However overall, our sample of gender-mismatched HT recipients fared as well as gender-matched patients in the vast majority of outcomes examined during the first year after HT surgery.

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What's New?

- Gender-mismatched HT patients with a male donor and a female recipient had more treated acute rejections and were rehospitalized a greater number of days after the surgical discharge during the first post-operative year, so these patients may need more intensive immunosuppression and closer monitoring for complications.
- There were no significant differences in: deaths, survival time, hospital length of stay for HT surgery, IV-treated infections, severe renal dysfunction, new-onset steroid-induced diabetes, cardiac allograft vasculopathy, or non-skin cancers, so gender-mismatched HT recipients fared as well as gender-matched patients in 8 of the 10 outcomes examined during the first postoperative year.
- HT recipients with higher cholesterol, severe renal dysfunction, diabetes, earlier treated rejection, or earlier IV-treated infection were at greater risk for decreased first-year survival, so these patients will need to be treated aggressively for these conditions to reduce the incidence of early death.

Figure 1. Flow chart showing how the sample size evolved for analysis of 347 heart transplant (HT) recipients.

Figure 2.

Kaplan-Meier survival curves during the first year after heart transplant surgery by donor-recipient gender group (N = 347). Log rank test not significant: 30-day survival: Group 1 = 95.2%, Group 2 = 87.5%, Group 3 = 94.1%; 1-year survival: Group 1 = 85.8%, Group 2 = 79.7%, Group 3 = 82.2%. Mean number of days survived during the first post-operative year: Group 1 = 326, Group 2 = 302, Group 3 = 320.

Table 1
Summary of previous research findings on significant outcomes in gender-mismatched heart transplant recipients

Outcome	Donor female - Recipient male	Reference	Donor male - Recipient female	Reference
Higher mortality	X	1-7, 9-12, 14, 20	X	2, 3, 9, 11
More acute rejections	X	4	X	10, 13
Worse graft survival	X	8, 12, 19		

Table 2
Baseline characteristics of 347 heart transplant patients by donor-recipient gender group

Characteristic ^a	Group 1 ^b (N = 273)	Group 2 ^b (N = 40)	Group 3 ^b (N = 34)	χ^2 or F ^c	P
Age at HT (years)	52.7 ± 9.6	52.8 ± 11.4	47.7 ± 12.0	3.81	.023
Minority race	33 (12.1)	5 (12.5)	13 (38.2)	16.66	.000
Urgent priority for HT	132 (48.4)	20 (50.0)	15 (44.1)	0.28	.869
Coronary artery disease	150 (54.9)	25 (62.5)	9 (26.5)	11.47	.003
Diabetes	50 (18.3)	9 (22.5)	6 (17.6)	0.43	.806
VAD or TAH	25 (9.2)	4 (10.0)	2 (5.9)	0.46	.794
IABP	22 (8.1)	3 (7.5)	1 (2.9)	1.14	.565
Ventilator	13 (4.8)	0	0	3.66	.160
IV inotropes	154 (56.4)	22 (55.0)	21 (61.8)	0.41	.814
Serum creatinine (mg/dl)	1.4 ± .5	1.5 ± .4	1.1 ± .3	7.36	.001
PRA >10%	22 (8.1)	4 (10.0)	3 (8.8)	0.18	.913
Ischemic time (minutes)	181 ± 58	182 ± 58	169 ± 60	0.67	.511
Donor age (years)	25.9 ± 9.2	31.9 ± 12.3	23.7 ± 8.8	8.46	.000
Repeat HT	14 (5.1)	1 (2.5)	0	2.29	.319
Patient BMI (kg/m ²)	25.5 ± 4.1	24.4 ± 3.9	23.9 ± 4.3	3.38	.035
Weight mismatch >20% ^d	77 (28.2)	13 (32.5)	14 (41.2)	2.56	.278
CMV mismatch ^e	31 (11.4)	11 (27.5)	2 (5.9)	9.79	.007
Smoking history	184 (67.4)	26 (65.0)	21 (61.8)	0.48	.786

BMI, body mass index; CMV, cytomegalovirus; HT, heart transplant; IABP, intra-aortic balloon pump; IV, intravenous; PRA, panel reactive antibody; TAH, total artificial heart; VAD, ventricular assist device.

^aCharacteristic is pre-HT unless otherwise noted.

^bGroup 1: same gender donor-recipient; Group 2: female donor-male recipient; Group 3: male donor-female recipient.

^cChi square (χ^2) was used for categorical variables, which are expressed as N (%); ANOVA (F) was used for continuous variables, which are expressed as mean ± standard deviation.

^dWeight mismatch >20% is based on the percent difference between patient weight and donor weight in kilograms using the formula of Costanzo-Nordin.²⁵

^eCMV mismatch: donor positive/patient negative.

Table 3
First-year outcomes in 347 heart transplant patients by donor-recipient gender group

Outcome	Group 1 ^a (N = 273)	Group 2 ^a (N = 40)	Group 3 ^a (N = 34)	χ^2 or F ^b	P ^c
Deaths	38 (13.9)	8 (20.0)	6 (17.6)	1.39	.498
Severe renal dysfunction ^d	93 (34.1)	19 (47.5)	6 (17.6)	8.51	.014
Steroid-induced diabetes	26 (9.5)	4 (10.0)	3 (8.8)	0.59	.744
CAV	19 (7.0)	3 (7.5)	4 (11.8)	0.07	.966
Non-skin cancers	10 (3.7)	0	2 (5.9)	5.48	.065
HT length of stay (days) ^e	20 ± 18	23 ± 14	18 ± 9	0.73	.571
Number of days rehospitalized ^e	23 ± 25	19 ± 19	38 ± 38	3.76	.005
Number of treated rejections	2.9 ± 2.7	2.3 ± 2.6	4.2 ± 3.7	4.11	.003
Number of IV-treated infections	1.5 ± 2.3	1.6 ± 3.1	1.5 ± 1.7	0.61	.652

CAV, cardiac allograft vasculopathy; HT, heart transplant; IV, intravenously.

^aGroup 1: same gender donor-recipient; Group 2: female donor-male recipient; Group 3: male donor-female recipient.

^bLogistic regression (χ^2), adjusting for patient age at HT and donor age, was used for dichotomous outcomes, which are expressed as N (%); MANCOVA (F), adjusting for patient age and donor age, was used for continuous outcomes, which are expressed as mean ± standard deviation.

^cSignificance determined at P .005.

^dDefined as a serum creatinine >2.5 mg/dL, a diagnosis of renal failure, or dialysis, using the definition of the International Society for Heart and Lung Transplantation registry report.²

^eN = 320: excludes 27 patients who died during the HT admission; Group 1 = 254; Group 2 = 34; Group 3 = 32.

Table 4
Cause of death for 52 of 347 patients (15.0%) who died during the first year after heart transplant surgery by donor-recipient gender group

Cause of death^a	Group 1^b (N = 273)	Group 2^b (N = 40)	Group 3^b (N = 34)	Total
Cytomegalovirus infection	7			7
Bacterial infection	4	2		6
Fungal infection	4		1	5
Protozoal infection	1			1
Acute rejection	3	2	2	7
Cardiac allograft vasculopathy	2	1		3
Right ventricular failure	2	1		3
Respiratory failure		1	1	2
Multi-organ failure	2	1		3
Lymphoma	3			3
Cerebral hemorrhage	2			2
Stroke	3			3
Myocardial infarction	1			1
Pulmonary embolism			1	1
Pancreatitis	1			1
Intra-operative pump failure	2		1	3
Intra-operative hemorrhage	1			1
Number (%) of deaths	38 (13.9)	8 (20.0)	6 (17.6)	52

^aSource: autopsy report (25) or death certificate (12) or physician note on the chart (15).

^bGroup 1: same gender donor-recipient; Group 2: female donor-male recipient; Group 3: male donor-female recipient.

Risk factors for decreased first-year survival in 347 heart transplant patients by donor-recipient gender group

Table 5

Risk factor ^a	Group 1 ^b (N = 273)	Group 2 ^b (N = 40)	Group 3 ^b (N = 34)	RR ^c (95% CI)	Wald	p ^d
Higher year 1 cholesterol (mg/dl)	220 ± 46	210 ± 54	226 ± 56		35.72	.000
Earlier IV-treated infection (days)	174 ± 158	126 ± 148	178 ± 152		15.39	.000
Severe renal dysfunction ^e	93 (34.1)	19 (47.5)	6 (17.6)	1.01 (1.00-1.02)	10.59	.001
Earlier treated rejection (days)	83 ± 119	85 ± 121	64 ± 115		7.86	.005
Diabetes (pre-existing & new-onset)	76 (27.8)	13 (32.5)	9 (26.5)	3.20 (1.41-7.27)	7.73	.005

CI, confidence interval; IV, intravenously; RR, relative risk.

^aFrom multivariate Cox regression. Categorical variables are expressed as N (%); continuous variables are expressed as mean ± standard deviation. Nonsignificant variables: pre-transplant cardiac diagnosis, total artificial heart or ventricular assist device before surgery, ventricular assist device after surgery, repeat heart transplant, patient age, patient gender, patient race, donor age, weight mismatch >20%, cytomegalovirus mismatch (donor positive/patient negative), cardiac allograft vasculopathy, respiratory failure, liver failure, stroke, non-skin cancers.

^bGroup 1: same gender donor-recipient; Group 2: female donor-male recipient; Group 3: male donor-female recipient.

^cRelative risk applies to dichotomous risk factors.

^dSignificance determined at P .005.

^eDefined as a serum creatinine >2.5 mg/dl, a diagnosis of renal failure, or dialysis, using the definition of the International Society for Heart and Lung Transplantation registry report.²