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Use of Cardiac Allografts With Mild and Moderate Left Ventricular Hypertrophy Can Be Safely Used in Heart Transplantation to Expand the Donor Pool

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Objectives The purpose of this study was to evaluate outcomes of heart transplantation (HTx) and changes in left ventricular wall thickness (LVWT) post-HTx using donors with left ventricular hypertrophy (LVH).

Background Limited data are available on use of donor hearts with LVH in HTx.

Methods We reviewed 427 patients who underwent HTx: 62 received hearts with LVH (interventricular septum [IVS] or posterior wall [PW] thickness ≥1.2 cm) by echocardiography, and 365 received hearts without LVH. The median follow-up was 3.8 years (range 0 to 16.2 years).

Results Recipient age was 56 ± 11 years and donor age was 30 ± 12 years. Baseline recipient characteristics were similar in both groups. Donors with LVH were older (35 ± 12 years vs. 29 ± 12 years, $p = 0.001$) and had higher rates of intracranial hemorrhage (38% vs. 15%, $p = 0.001$). The LVWT was increased in the LVH group compared with LVWT in the non-LVH group (IVS: 1.28 ± 0.18 cm vs. 0.85 ± 0.19 cm, PW: 1.27 ± 0.19 cm vs. 0.85 ± 0.20 cm, $p = 0.0001$ for both groups). Mild LVH (1.2 to 1.3 cm) was found in 42%, moderate (>1.3 to 1.7 cm) in 53%, and severe (>1.7 cm) in 5% of donors with LVH. Left ventricular wall thickness regression occurred in both IVS and PW (1.28 ± 0.18 cm vs. 1.10 ± 0.13 cm vs. 1.13 ± 0.14 cm, and 1.27 ± 0.19 cm vs. 1.11 ± 0.11 cm vs. 1.13 ± 0.14 cm, at baseline, 1 year, and 5 years, respectively; $p < 0.001$ for change from baseline to 1 and 5 years for both locations). Patients with or without donor LVH had similar 1-year (3.5% vs. 9.5%, $p = 0.2$) and 5-year survival rates (84 ± 5.9% vs. 70 ± 2.7%, $p = 0.07$).

Conclusions Short- and long-term survival rates and rates of LVH at follow-up were similar in both groups, suggesting that donor hearts with mild and moderate LVH can be safely used in HTx. (J Am Coll Cardiol 2008;51:1214–20)

Heart transplantation (HTx) provides definitive therapy for patients with end-stage congestive heart failure. Although improved preservation techniques and post-HTx immunosuppression have significantly improved outcomes, the number of patients on waiting lists has progressively increased over the last decade (1–3). Although initially strict donor and recipient selection criteria were established, liberalization of donor selection criteria and ways of expanding the donor pool have been suggested (4–7). Use of donor hearts with left ventricular hypertrophy (LVH) has varied among transplant centers, and there is little information concerning transplantation of donor hearts with LVH.

Until recently, only 2 small studies have been published and found that the presence of LVH in the donor heart was associated with early graft dysfunction and lower survival (8,9). Moreover, there are no data regarding the changes in measured wall thickness after HTx in this patient population. Given that use of donor hearts with LVH may permit an expansion of the donor pool, we aimed to review our experience with HTx using donors with LVH and to evaluate the changes in LVH over time.

Methods

Patients. We retrospectively reviewed 427 consecutive HTx donors and recipients between 1989 and 2004 at Cedars-Sinai Medical Center. Recipients younger than 16 years of age and those with combined heart-lung transplan-

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tation were excluded. The donor and recipient evaluation and rejection surveillance have been described elsewhere (10). The post-HTx regimen included induction therapy consisting of OKT3 or Thymoglobulin. Maintenance immunosuppressive therapy included cyclosporine or tacrolimus, azathioprine or mycophenolate mofetil, and prednisone.

Donor hearts were preserved using a cold infusion of University of Wisconsin solution or Stanford solution prior to 2000. HTx was performed using the total orthotopic (bicaval) technique in 85% of recipients.

Definition and grading of LVH. Left ventricular hypertrophy was quantitatively assessed by echocardiography using wall-thickness measurements according to American Society of Echocardiography recommendations (11). Left ventricular hypertrophy was defined as interventricular septum (IVS) and/or posterior wall (PW) thickness ≥1.2 cm. Mild LVH was defined as wall thickness of 1.2 to 1.3 cm, moderate LVH as 1.4 to 1.7 cm, and severe LVH as >1.7 cm. Follow-up echocardiograms at 1 and 5 years post-HTx were available in 66% and 49% of patients, respectively. The electrocardiogram (ECG) definition of LVH was based on standard voltage criteria: SV1 + RV5 or RV6 >35 mm.

Statistical analysis. Results for continuous variables are presented as mean ± SD and for categorical variables as frequency (percentage). The comparison of continuous variables between groups was made using *t* test or the Wilcoxon rank sum test as appropriate. Categorical variables were compared using chi-square or Fisher exact tests. Within-group change in numerical variables across 2 time points was assessed by the Wilcoxon signed rank test. Within-group change in dichotomous variables across 2 time points was assessed by the McNemar test for related proportions. Survival estimates were generated by the Kaplan-Meier method. The log-rank and Wilcoxon tests were used to compare survival across groups. Multivariable stepwise Cox proportional hazards models were employed to assess variables associated with the risk of death. All statistical tests were two-sided, and a significance level of 0.05 was used throughout. Statistical analyses were performed using the SAS system version 9.1 (SAS Institute Inc., Cary, North Carolina).

Results

Donor and patient characteristics. Sixty-two patients received a donor heart with LVH, and 365 received a heart without LVH. Median follow-up was 3.8 years (range 0 to 16.2 years).

Donors with LVH were significantly younger ($p = 0.0003$) and had a higher prevalence of intracranial bleeding ($p = 0.02$) (Table 1). No significant differences were observed in terms of other baseline characteristics. Twenty-nine donors (48%) had history of hypertension (HTN). Among donors with LVH, 42% of patients had mild, 53% had moderate, and 5% had severe LVH as determined by echocardiography. Twenty-five (40%) donors also had evidence of LVH by as determined by ECG.

Baseline pre-HTx recipient characteristics were similar in the 2 groups and are presented in Table 1. The post-HTx recipient characteristics are presented in Table 2. A long (>240 min) ischemic time was found only among patients who received allografts without LVH (6%). A larger number of patients with donor LVH were treated with tacrolimus ($p = 0.004$). No significant differences were found in terms of length of hospitalization, acute cellular rejection ≥3A, and cytomegalovirus infection rates.

Abbreviations and Acronyms

ACEI = angiotensin-converting enzyme inhibitor
ARB = angiotensin receptor blocker
HTN = hypertension
HTx = heart transplantation
IVS = interventricular septum
LV = left ventricular
LVH = left ventricular hypertrophy
LVWT = left ventricular wall thickness
PW = posterior wall

Survival analysis. No significant differences in 30-day and 1-year mortality were found between recipients of donor heart with LVH compared with those without LVH (1.6% vs. 3.3%, $p = 0.2$, and 3.5% vs. 9.5%, $p = 0.7$, respectively). The overall survival of the 2 groups is shown in Figure 1 and reveals no significant difference ($p = 0.07$) (Fig. 1A). Multivariable stepwise Cox proportional hazards analysis found evidence that donor LVH was associated with a reduced death hazard rate. The independent predictors of mortality are shown in Table 3.

Prior studies have demonstrated lower survival in recipients of older donor hearts (12). We divided both groups, with and without donor LVH, by donor age <45 years (younger) and ≥45 years (older). Survival analysis revealed a trend ($p = 0.08$) (Fig. 1B) indicating a possible difference among recipients of younger donors with or without donor LVH and older donors with or without LVH.

A separate analysis comparing survival among patients who received hearts with mild LVH or moderate or severe LVH did not reveal significant differences ($p = 0.82$). No significant difference in survival between recipients with donor LVH as determined by both ECG and echocardiography and those with donor LVH determined only by ECG evidence was observed ($p = 0.58$) (Fig. 2A). For about the first 2.5 years post-transplant, almost identical survival was observed among recipients of donor LVH with and without donor history of HTN; however, those with donor history of HTN have a trend for worse survival thereafter ($p = 0.05$) (Fig. 2B).

One hundred sixty-two patients died over the follow-up period: 13 patients (1 within 30 days) in the LVH group and 149 (12 within 30 days) of those in the group without LVH. The causes of late deaths were right ventricular failure (3%), rejection (10%), cardiac (36%), and noncardiac (51%). Compared with recipients of allografts without