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Heart transplant outcomes in patients with left ventricular non-compaction cardiomyopathy

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BACKGROUND: Left ventricular non-compaction cardiomyopathy (LVNCC) is a rare disease that starts in utero and may progress to heart failure (HF), sometimes requiring orthotopic heart transplantation (OHT). There are limited data addressing characteristics of LVNCC patients that require OHT and their outcomes. We therefore sought to investigate the characteristics and outcomes of LVNCC patients treated with OHT.

METHODS: We queried the United Network for Organ Sharing (UNOS) database for all patients listed for OHT with LVNCC as the primary heart failure etiology between 2000 and 2013. We examined their characteristics at listing and outcomes after OHT and compared the findings with those of patients with idiopathic cardiomyopathy (IDCMP).

RESULTS: We identified 113 patients (43 adults and 70 pediatrics) with LVNCC of 45,298 patients (0.25% overall, 0.11% of adults and 1.0% of pediatrics) listed for OHT in this time period. Most were male children with mean age at listing of 16.9 years. Compared with the overall IDCMP cohort, patients with LVNCC were younger, had higher use of inotropes and extracorporeal membrane oxygenation (ECMO), and were more often listed as UNOS Status 1A with shorter waiting time. However, when adjusted for age, gender and ethnicity, these differences disappeared. During transplant listing, 8 (7.9%) died, 5 (5.0%) improved and avoided transplant, 3 (3.0%) became too sick for transplant and 78 (77.2%) underwent OHT. There was a non-significant trend toward longer cardiac allograft survival in patients with LVNCC (10.6 vs 9.4 years; log-rank test, $p = 0.068$). Patients with LVNCC had similar outcomes to other IDCMP patients, except for more post-transplant infections (50.0% vs 21.6%, $p < 0.05$).

CONCLUSIONS: LVNCC patients undergoing heart transplantation are mostly pediatric and predominantly bridged to transplant with inotropes or ECMO. Despite having more post-transplant infections, their survival is similar to that of other IDCMP patients.

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Left ventricular non-compaction cardiomyopathy (LVNCC) is a rare form of cardiomyopathy that starts in utero and may progress throughout life,[1,2] sometimes requiring advanced heart failure (HF) therapy and orthotopic lung transplantation (OHT). Although the true prevalence of this disease is unknown, it is found in 0.26% of all echocardiograms, and in 3% to 4% of patients with left ventricular (LV) systolic dysfunction.[3,4] There appears to be no gender predominance[5] and HF symptoms affect both

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children and adults. Although its pathogenesis is incompletely understood, LVNCC is thought to occur during in utero cardiac development and be associated with several genes.[6–8] Pathologically, LVNCC is characterized by hypertrabeculations and non-compacted myocardium in the LV. Patients usually present with symptoms of HF, systemic embolism or arrhythmias.[9] However, there is a wide phenotypic spectrum with variable extent and nature of cardiac involvement.[10] The natural course of this disease is variable but associated with mortality of up to 47% within 6 years of diagnosis. LVNCC is a progressive disease and may lead to heart failure in 25% of pediatric cases.[11] Adult patients appear to have a more acute presentation, with dyspnea in about 80% and New York Heart Association (NYHA) Class III/IV HF symptoms in 35%.[12] OHT is performed in 4% to 14% of patients with LVNCC,[9,11,12] but post-transplant outcomes are largely unknown.

We therefore sought to describe the characteristics and outcomes of patients with LVNCC treated with OHT and compared the findings to those of patients with idiopathic cardiomyopathy (IDCMP).

Methods

We queried the United Network for Organ Sharing (UNOS) registry, a voluntary, self-reported database of OHT in the United States, for all patients with LVNCC as their primary HF etiology between 2000 and 2013. We examined their characteristics and outcomes after OHT and compared them to those with IDCMP. We defined pediatric as ≤ 18 years of age and adult as >18 years of age.

All continuous variables are described as mean and standard deviation and compared using a *t*-test. Categorical variables are described as frequency and percent whenever appropriate, and comparison was done using chi-square tests. Significantly different factors were adjusted for age, gender and ethnicity using binary logistic regression analysis (adjusted *p*-value). Survival analyses were performed using the Kaplan-Meier method and multivariate Cox proportional hazard models. We utilized SPSS version 19.0 (IBM SPSS) for all statistical analyses.

Results

Of 45,298 patients listed for OHT, we identified 113 LVNCC patients (43 adults and 70 pediatrics), of whom 78 (77.2%) underwent OHT, and 14,313 patients with IDCMP. Overall, LVNCC constituted 0.25% of the listed (0.11% of adults and 1.0% of pediatrics) and 0.3% of transplanted patients. Sixty percent were pediatric patients, with a mean age at listing of 16.9 years (median 13 years, range 0 to 69 years, standard deviation 19.2 years). Of these, 37 (32.7%) patients were listed within the first year of life, and another 33 from age 2 to 18 years (Figure 1). Compared with 14,313 IDCMP patients from the same period, LVNCC patients were much younger (16.9 vs 44.6 years of age, $p < 0.001$), predominantly non-white (57.5% vs 43%, $p < 0.01$) and less predominantly male (54.9% vs 69.8%, $p < 0.01$). Unadjusted comparison to the older cohort of IDCMP patients showed increased use of inotropes (50.4% vs 39.9%, $p < 0.05$) and extracorporeal membrane oxygenation (ECMO) (3.5% vs 1.2%, $p < 0.05$), as well as less utilization of automated internal cardiac defibrillation (ICD) at time of listing (37.2% vs 60.9%, $p < 0.001$). However, once adjusted for age, gender and ethnicity, these differences disappeared and adjusted *p*-values no longer showed statistical significance. Patients with LVNCC were more often listed as Status 1A (54.0% vs 25.8%, $p < 0.001$) and had a shorter waiting period (189.4 vs 279.5 days, $p < 0.05$) than other IDCMP patients (Table 1). Hemodynamic profiles were similar between listed LVNCC and IDCMP patients (Table 2). At the end of the study period, 101 patients were removed from the transplant list (transplanted, died, too sick for transplant, recovery). During listing, 5 (5%) improved and did not require OHT, 3 deteriorated and became too sick for transplant, and 8 (7.9%) died. Causes of death were cardiac arrest in 3, ventricular failure in 1, cerebrovascular hemorrhage in 1, multiple-organ failure in 1 and unknown or unspecified in 2 (Table 3).

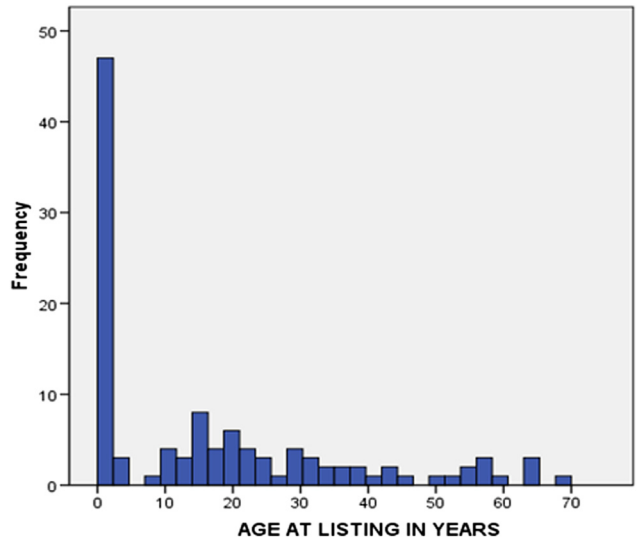

Figure 1 Age distribution at listing.

Seventy-eight patients (77.2%) underwent OHT (compared with 68.2% of IDCMP, adjusted $p = 0.04$). There was a non-significant trend toward longer graft survival in patients with LVNCC (10.6 vs 9.4 years, log-rank test, $p = 0.068$) (Figure 2). There was also no difference in graft survival between adult (log-rank test, $p = 0.11$) and pediatric (log-rank test, $p = 0.11$) patients.

Survival was not predicted by age, gender, or panel-reactive antibody (PRA); however, HLA mismatch was associated with worse survival (hazard ratio [HR] 1.08, 95% confidence interval [CI] 1.012 to 1.152, $p < 0.05$). Post-OHT outcomes were similar between the two groups, with the exception of increased rates of infections treated with intravenous antibiotics in LVNCC patients (50% vs 21.6%, $p < 0.05$) (Table 4).

Discussion

To our knowledge, this is the first and largest report describing the characteristics and outcomes of patients with LVNCC and end-stage HF treated with OHT. We have shown that patients with HF from LVNCC benefit from OHT and are mostly non-white male children who require