Journal of Cardiac Failure Vol. ■■ No. ■■ 2016

Clinical Investigation

Survival After Heart Transplantation in Patients With Arrhythmogenic Right Ventricular Cardiomyopathy

EUGENE C. DEPASQUALE, MD, RICHARD K. CHENG, MD, MARIO C. DENG, MD, ALI NSAIR, MD, WILLIAM J. MCKENNA, MD, GREGG C. FONAROW, MD, AND DANIEL L. JACOBY, MD

Los Angeles, California

ABSTRACT

Background: Outcomes of arrhythmogenic right ventricular cardiomyopathy (ARVC) patients after heart transplantation have not been well studied. Diagnostic criteria were established in 1994 and subsequently revised in 2010. We sought to better characterize this population in a national cohort.

Methods: A total of 35,138 heart transplant–only recipients were identified from the United Network for Organ Sharing (UNOS) Thoracic Registry (1994–2011); 73 had ARVC. The non-ARVC group included ischemic cardiomyopathy, restrictive cardiomyopathy, dilated cardiomyopathy, hypertrophic cardiomyopathy, and other. Survival was censored at 12 years. Multivariate Cox proportional hazard regression analysis was adjusted for age, sex, DM, race, ischemia time, dialysis, life support, wait time, and HLA mismatch.

Results: There were 73 ARVC and 35,065 non-ARVC patients. The ARVC cohort was associated with less ventricular assist device use ($P = .001$) and significantly decreased pulmonary arterial and capillary wedge pressures ($P < .001$). Survivals at 1, 5, and 10 years were, respectively, ARVC 87%, 81%, and 77%, and non-ARVC 87%, 72%, and 53% (log rank $P = .07$). The ARVC unadjusted hazard ratio for all-cause mortality was 0.59 (95% confidence interval [CI] 0.34–1.04; $P = .073$). Multivariate analysis yielded a hazard ratio of 0.68 (95% CI 0.35–1.30; $P = .25$). ARVC survival was similar to restrictive, hypertrophic, and dilated cardiomyopathies and significantly better than ischemic cardiomyopathy.

Conclusions: This is the largest reported series of ARVC after heart transplantation, of which 11% were pediatric. Survival was similar to the non-ARVC cohort, with improved survival over ischemic and restrictive etiologies. (*J Cardiac Fail 2016;*■■*:*■■–■■)

Key Words: Arrhythmogenic right ventricular cardiomyopathy, cardiomyopathy, heart transplantation, outcomes.

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a primary heart muscle disorder characterized by ventricular arrhythmias with concomitant progressive myocardial loss with fibrous or fibrofatty replacement, primarily of the right ventricle, with with involvement of the left ventricle at later stages.[1,2] Diagnostic criteria were formally established in 1994 with subsequent revision in 2010 aimed at improving sensitivity for early and familial disease.[3,4] The prevalence of ARVC is estimated to be ~1:1000–1:5000, although age-dependent penetrance and variable expression make the true prevalence difficult to determine. Inheritance is mainly autosomal dominant, with rare recessive forms noted as well.[1,5] The clinical course of ARVC is variable and marked by ventricular arrhythmias, sudden death, and heart failure. Though ARVC is typified by ventricular arrhythmias, heart failure incidence as high as 20% has been reported.[6,7]

Outcomes with heart transplantation for this population have been previously reported, with the largest single-center series

From the UCLA Advanced Heart Failure, Heart Transplantation & Mechanical Circulatory Support Program, David Geffen School of Medicine at UCLA, Los Angeles, California.

Manuscript received January 9, 2016; revised manuscript received April 16, 2016; revised manuscript accepted April 25, 2016.

Reprint requests: Eugene C. DePasquale, MD, UCLA Advanced Heart Failure, Heart Transplantation & Mechanical Circulatory Support Program, David Geffen School of Medicine at UCLA, 100 UCLA Medical Plaza, Suite 630 East, Los Angeles, CA 90095. Tel: +310 825 6908; Fax: +310 825 9013. E-mail: edepasquale@mednet.ucla.edu.

Funding: This work was supported in part by Health Resources and Services Administration contract 234-2005- 370011C. The content is the responsibility of the authors alone and does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the US Government.

See page ■■ for disclosure information.

1071-9164/$ - see front matter

© *2016 Elsevier Inc. All rights reserved.*

http://dx.doi.org/10.1016/j.cardfail.2016.04.020

consisting of 18 patients from the Johns Hopkins ARVD Program Registry. In that population, a majority (72%) received transplants owing to heart failure symptoms (biventricular failure [n = 4], right ventricular failure [n = 9]), with the remainder undergoing transplantation because of ventricular arrhythmia. One-year post-transplantation survival was 94%.[8]

The aim of the present study was to ascertain the prevalence, clinical characteristics, and outcomes of ARVC patients in a national cohort undergoing heart transplantation.

Methods

Selection and Identification of Patients

Transplant centers in the United States are required to report clinical and demographic data to the Organ Procurement and Transplantation Network Registry, which is operated by the United Network of Organ Sharing (UNOS). Analysis was limited to patients in the UNOS Thoracic Registry who underwent heart transplantation from January 1994 to December 2011. Analysis was further limited to first-time single-organ heart-only transplant recipients. Patients with repeated cardiac transplants or multiorgan transplants were excluded from the study.

Baseline clinical characteristics of the study population were obtained from the UNOS Thoracic Registry. The cohort was then divided into ARVC and non-ARVC groups according to the Heart Transplant Recipient Registration Worksheet. The non-ARVC groups consisted of 5 subgroups of patients: (1) ischemic cardiomyopathy (ie, predominant etiology of heart failure due to coronary heart disease); (2) dilated cardiomyopathy (ie, idiopathic, viral, postpartum, or familial); (3) hypertrophic; (4) restrictive cardiomyopathy; and (5) other (ie, congenital or valvular heart disease).

There were no patients diagnosed with ARVC before 1994. A similar proportion of ARVC (2, 2.7%) and non-ARVC (2796, 7.4%) patients were lost to follow-up and excluded.

Statistical Analyses

Patient demographic and clinical characteristics of the cohort were first compared by diagnosis (ARVC). For continuous variables, the mean and SD were calculated, and for categoric variables, proportions or percentages were calculated. For unadjusted comparisons between groups, the 2-sample *t* test was used for continuous variables and the Fisher exact test was used for categoric variables. For multiple-group comparisons, the analysis of variance test was used for continuous variables and the Fisher exact test for categoric variables.

Follow-up duration was censored at 12 years (144 months) for mortality analysis. The most recent follow-up was determined as the last clinic visit entered into the database and was defined as time from transplantation to death or last clinic visit. Noncardiovascular death was defined as primary graft failure, rejection, infection, malignancy, multiorgan failure, and other. For descriptive purposes, crude cumulative mortality rates were estimated and plotted with the use of the Kaplan-Meier method and compared between groups by means of the log-rank test. Cox proportional hazards regression models were used to estimate association of ARVC with mortality for several scenarios including (1) without any adjustment, (2) without any adjustment and consideration of time-varying effect of ARVC, (3) adjustment for previously established pre- and post-transplantation risk factors without time-varying effect, and (4) adjustment for previously established pre- and post-transplantation risk factors without time-varying effect.

Previously established pre- and post-transplantation risk factors were adjusted with the use of Cox regression models. Pre-transplantation variables included recipient sex, recipient age, body mass index, duration on the transplant waiting list, UNOS status, serum creatinine, peak panel reactive antibody, human leukocyte antigen (HLA) mismatch, need for life support (including pre-transplantation intra-aortic balloon pump, ventricular assist device, extracorporeal membrane oxygenation, and/or ventilator). Transplantation variables included donor age and ischemia time. A backward stepwise elimination procedure was used to identify the final multivariable models, starting with a set of potential covariates known to be associated with post-transplantation mortality. Variables were included when their significance level was ≤ 0.05. The proportional hazards assumption was tested for variables in the models by means of time-varying covariates. Visual inspection of log(–logS(t)) versus log t plots across primary categoric variables did not indicate serious violations to the proportional hazards assumptions. Final variables included age, sex, diabetes, ischemia time, dialysis, life support, duration on the transplant waiting list, and HLA mismatch.

Results

Prevalence

During the study period, 35,138 patients underwent cardiac transplantation, including 73 (0.2%) ARVC patients and 35,065 non-ARVC patients (ischemic cardiomyopathy, n = 14,279, 40.6%; dilated cardiomyopathy, n = 15,249, 43.4%; restrictive cardiomyopathy, n = 764, 2.2%; hypertrophic cardiomyopathy, n = 595, 1.7%; other, n = 4178, 11.9%). For the 35,138 patients included in the analysis, mean follow-up time for the study was 66 ± 56 months.

Clinical and Demographic Profile of the Study Group

The clinical and demographic characteristics of the overall study population are presented in Table 1. Compared with the non-ARVC transplant recipients, ARVC transplant patients were not significantly younger (42 ± 18 y vs 46 ± 19 y; $P = .068$) but were less likely to have diabetes (3% vs 19%; $P < .0001$) and less likely to have a history of smoking (21% vs 39%; $P = .001$). ARVC patients were also significantly less likely to be bridged to transplant with the use of mechanical circulatory support (5.5% vs 20%; $P = .001$) with left ventricular assist device (LVAD; n = 1), right ventricular assist device (n = 1), or biventricular assist device (n = 1) use. Pulmonary arterial systolic (25 ± 7 mm Hg vs 43 ± 15 mm Hg; $P < .001$), pulmonary arterial diastolic (13 ± 6 mm Hg vs 21 ± 9 mm Hg; $P < .001$), and pulmonary capillary wedge

Download English Version:

https://daneshyari.com/en/article/5614090

Download Persian Version:

https://daneshyari.com/article/5614090

Daneshyari.com