HEART FAILURE AND TRANSPLANTATION
Journal Watch
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REVIEWS:

Frazier OH et al. "Ventricular reconditioning and pump explantation in patients supported by continuous-flow left ventricular assist devices." *J Heart Lung Transplant* 2015;34:766-772.

This is a retrospective study of a small cohort of patients who underwent successful explantation of their LVAD. The authors review their strategy of assessing for readiness for weaning and actual weaning process as well as the merit of this strategy. The study, which covers time between 2006-2014 during which about 657 patients underwent LVAD implantation. All of these implantations were for NYHA class 4, chronic heart failure as DT or BTT. The general approach for these patients at the institute was to place an LVAD (generally HMII or HVAD), optimize medical therapy, and discharge home when ready. The initial approach was to maximize LV unloading with the VAD. These patients were then followed systematically as outpatients and evaluated, generally with an echocardiogram, to optimize VAD settings as needed.

A small subset of this larger group underwent LVAD weaning trials after a variable duration of VAD support. Indications for a weaning trial to attempt explantation were generally based on the opinion of the medical team, improvements noted in LV function, likelihood for complications, as well as based on patient desire (to not undergo transplantation and have the VAD weaned off).

During the weaning trial, the key assessment component was the opening of the aortic valve (for duration of cardiac cycle) with pump wean. The pump RPMs were turned down transiently to 6000 RPM, and the aortic valve opening was assessed. The goal was to start with an aortic valve opening of 10% (of the cardiac cycle). This allowed for VAD to function in parallel to the LV rather than in series. LV size assessment was key during this stage – to ensure LV size improvement compared to pre-implantation assessment. These patients were then slowly weaned to minimal permissible speeds to allow reloading and potentially remodeling of the LV to take place. Once aortic valve opening of 33% was achieved, the patients were deemed reasonable candidates for explantation. Post explantation, they were continued to be managed with medical HF therapy.

With this approach, about 30 patients were evaluated for explantation, and 27 were successfully weaned. The authors describe modification of the surgical technique for explantation over time, including a minimally invasive approach that involves leaving an inactive pump in situ. Most of these patients continued to be in NYHA class I to II on medical therapy after an extended follow-up.

Although the study only represents about 4% (27/657 total LVAD patients), it does lay down the foundation for some potential principles in long term management of LVAD patients. It was noted that the patients who underwent successful explantation demonstrated statistically significant improvements in cardiac output, cardiac index, PCWP, mean PA pressure, LVEDD and LVEF between pre-implantation and pre-explantation time periods after a mean LVAD support duration of 532±423 days.

The concept of LV unloading as a potential therapy for chronic heart failure is well established. This period of reduced workload, reduced myocardial metabolic demand and improved net cardiac output (effective coronary perfusion) as a result of LVAD implantation can break the cycle of chronic heart failure begetting more heart failure. This period of quiescence may allow for positive remodeling of the ventricle and potentially allow time for medical therapy to start showing its benefits.

Therefore, it is not unreasonable to suggest that, in some patients; the VAD may be therapeutic to the point of meaningful recovery and therefore allow explantation. Authors stress the point of using therapeutic reconditioning even in stable HF patients.

Given the improvements in technology and durability as well as the gain in experience, VAD implantation has already become standard therapy for advanced heart failure. However, the majority of these implantations continue to be under BTT or DT strategies. Thus, once a stable status is achieved, there is very little incentive for weaning trials. This is in the face of continued issues of morbidity and mortality directly related to the VAD itself (stroke, bleeding, infections, etc). As this study points out, in some patients, actively assessing for weaning eligibility and allowing for LV reloading after adequate therapeutic time should be considered. When such an active approach is adopted, the number of eligible patients may be greater than the 4% population described here. Furthermore, due to an understandable era bias, there were very few HeartWare HVAD patients in this study. It would be valuable to gather data about an optimal weaning plan for HVAD patients too.

Al-Kindi SG et al. "Heart transplant outcomes in patients with left ventricular non-compaction cardiomyopathy." ***J Heart Lung Transplant*** **2015;34:761-765.**

This is an analysis the United Network for Organ Sharing (UNOS) database of patients listed for orthotopic heart transplant with a primary diagnosis of left ventricular noncompaction (LVNCC). The study described the demographics, hemodynamics, and outcomes before and after transplant, and survival for patients listed for LVNCC compared to idiopathic dilated cardiomyopathy (IDCMP). The study identified 45,298 patients listed for heart transplant in the UNOS database. Of those, 113 patients were diagnosed with LVNCC. 43 were adults (38%), and 70 were pediatric patients (62%).

Of the 113 patients, 101 patients were removed from the waiting list. 78 patients (77%) underwent heart transplant (HTx), 5 patients (5%) improved and did not require HTx, 3 (3%) became too sick for HTx, 3 patients (3%) were transferred to another center, 8 patients (8%) died, and 4 patients (4%) did not undergo HTx for other reasons. Causes of death included cardiac arrest (3), ventricular failure (1), cerebrovascular accident (1), multiorgan failure (1), and unknown (1).

The mean age at listing was 16.9 years with a median age of 13 years. 37 patients were listed within the first year of life, and 33 patients listed from age 2 to age 18 years. Compared to 14,313 patients with IDCMP, LVNCC patients were younger (mean age 16.9 vs. 44.6 years of age), less often white (43% vs. 57%), and less often male (54.9% vs. 69.8%).

Using multifactor analysis and an unadjusted comparison, LVNCC patients had an increase use of inotropes (50.4% vs. 39.9%), ECMO at listing (3.5% vs. 1.2%), ECMO at transplant (4.0% vs. 0.9%), and a lower utilization of AICDs (37.2% vs. 60.9%). When adjusted for age, gender, and ethnicity, those differences disappeared. LVNCC patients also had less utilization of IABP at listing (0% vs. 4.1%).

LVNCC patients were more often listed as Status 1A (54% vs. 25.8%) and less often listed as a Status 1B (21% vs. 36%) or Status 2 (22% vs. 36%). LVNCC patients also had a shorter wait time (189.4 vs. 279.5 days).

As to be expected, an HLA mismatch was associated with worse survival with a HR of 1.08 (CI 1.012 to 1.152). Post HTx outcomes were similar between the two groups except for increase rates of drug treated infection in the LVNCC group (50% vs. 21.6%).

This is a well-designed study of patients listed for heart transplant with a diagnosis of noncompaction cardiomyopathy. This study compared patients with LVNCC to those with IDCMP after they have been listed for transplant.

This study utilizes the UNOS database, thus providing a large cohort of patients. However, the sample population of patients with LVNCC (0.25% of listed patients and 0.3% of transplanted patients) was small.

Also, the authors are limited to the data available in the UNOS registry. Patients with LVNCC are younger on average than patients with IDCMP. There was a mean age difference of 27.7 years between the 2 groups.

Differences between the 2 groups (LVNCC and IDCMP) were found in an unadjusted cohort. With control for age, gender, and ethnicity, the difference was not found to be statistically significant. The authors do not clarify if an individual model was used for age, gender, and ethnicity individually.

The authors correctly identify that there may be a bias as patients who are not referred or listed for HTx would not be included in this study. This may include patients on either spectrum who are either too well or too sick to undergo HTx.

LVNCC patients were more often listed as Status 1A. This may reflect pediatric (under age 18) listing criteria as well as level of illness at listing. LVNCC also had a shorter wait time, which is most likely a reflection of Status 1A listing.

LVNCC is increasingly recognized as a type of congenital cardiomyopathy. This study suggests that patients listed for HTx due a diagnosis of LVNCC have survival and outcomes similar to those with IDCMP.

ADDITIONAL ARTICLES OF INTEREST:

JACC-Heart Failure:

Carson PE, et al. The Hospitalization Burden and Post-Hospitalization Mortality Risk in Heart Failure With Preserved Ejection Fraction: Results From the I-PRESERVE Trial (Irbesartan in Heart Failure and Preserved Ejection Fraction). JACC Heart Failure. Volume 3(6). June 1, 2015. 429-441.

American Journal of Transplantation:

••Madariaga M, Michel S, Madsen J, et al. Kidney-Induced Cardiac Allograft Tolerance in Miniature Swine is Dependent on MHC-Matching of Donor Cardiac and Renal Parenchyma. American Journal of Transplantation. June 2015;15(6):1580-1590.

This is an important investigational study looking at inducing cardiac allograft tolerance by using a simultaneous kidney transplantation with varying combinations of MHC matching / mismatching between the organs and the donor-recipients in a swine model. The study suggests that MHC matching between the kidney and the cardiac graft (irrespective of recipient match) was associated with less rejection, longer graft survival via induction of tolerance.

Pediatric Transplantation:

••Loiselle K, Gutierrez-Colina A, Blount R, et al. Longitudinal stability of medication adherence among adolescent solid organ transplant recipients. Pediatric Transplantation [serial online]. June 2015;19(4):428-435.

Study assess the very daunting problem of medication adherence in young transplant patients, sheds some light on the actual burden, impact and suggests that frequent monitoring may be the only available viable option to keep a check on the issue.

Journal of the American College of Cardiology:

Bharucha T, et al. Sudden Death in Childhood Cardiomyopathy. Results From a Long-Term National Population-Based Study. JACC. Volume 65 (21), June 2, 2015. 2302-2310.

Mancini D, Colombo PC. Commentary by Fuster V. Left Ventricular Assist Devices. A Rapidly Evolving Alternative to Transplantation. JACC. Volume 65 (23), June 16 2015. 2542-2555

Forman DE, et al. Heart Failure as a Newly Approved Diagnosis for Cardiac Rehabilitation. JACC. Volume 65 (24), June 23 2015. 2652-2659.

Journal of Heart and Lung Transplantation:

Dean et al. Reduction in driveline infection rates: Results from the HeartMate II Multicenter Driveline Silicone Skin Interface (SSI) Registry. J Heart Lung Transplant, Volume 34, Issue 6, June 2015, Pages 781-789

Roig et al. Heart transplantation using allografts from older donors: Multicenter study results. J Heart Lung Transplant, Volume 34, Issue 6, June 2015, Pages 790-796

Robertson et al. Concomitant aortic valve procedures in patients undergoing implantation of continuous-flow left ventricular assist devices: An INTERMACS database analysis. J Heart Lung Transplant, Volume 34, Issue 6, June 2015, Pages 797-805

••Simmonds et al. Outcome of shared care for pediatric cardiac transplantation between two nations with different health care systems. J Heart Lung Transplant, Volume 34, Issue 6, June 2015, Pages 806-814

••Khuu et al . Reduced HLA Class II antibody response to proteasome inhibition in heart transplantation. J Heart Lung Transplant, Volume 34, Issue 6, June 2015, Pages 863-865

Birks EJ, et al. An examination of survival by sex and race in the Heartware Ventricular Assist Device for the Treatment of Advanced Heart Failure (ADVANCE) Bridge to Transplant (BTT) and continued access protocol trials. J Heart Lung Transplant 2015; 34: 815-824.

Morris AA, et al. Race and ethnic difference in the epidemiology and risk factors for graft failure after heart transplantation. J Heart Lung Transplant 2015; 34: 825-831.

Schmitto JD, et al. First implantation in man of a new magnetically levitated left ventricular assist device (HeartMate III). J Heart Lung Transplant 2015; 34: 858-860.