Reduced Myocardial Brain Natriuretic Peptide Expression and Collagen Deposition Following Ventricular Assist Device Support for Heart Failure

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Background: Unloading of the myocardium with ventricular assist devices (VADs) induces adaptive remodeling potentially through alterations in extracellular matrix components. A biochemical marker of volume overload, pathologic hypertrophy, and ventricular dysfunction, brain natriuretic peptide (BNP) plasma levels are reduced following VAD therapy and may herald myocardial functional recovery. However, the role of tissue BNP in response to mechanical unloading of the failing myocardium is unclear. We investigated the relationship between myocardial expression of BNP, pro-alpha 1(II) collagen (COL I A2), and transforming growth factor beta (TGF-B), a known regulator of vascular fibrosis, in the setting of cardiac unloading.

Methods: Left ventricular myocardium from 11 patients with end stage heart failure was obtained at the time of VAD implantation and at cardiac transplant. Etiologies for heart failure included ischemic disease (43%), idiopathic dilated (6%), ischemic (4%), and hypertrophic (1%) cardiomyopathy. VAD treatment duration ranged from 4 to 1086 (Mean 96) days. Real-time quantitative PCR was used to determine differential expression of BNP, TGF-B, and COL IA2. PCR results were reported as the mean threshold cycle normalized for expression of an internal control (ribosomal 18s protein). Specimens were evaluated by a blinded pathologist for vascular fibrosis and reported on a scale from 0 to 3 (3 = Severe). Statistical significance in differential expression of BNP, TGF-B, and COL IA2 expression post-VAD was assessed using a paired student’s t-test.

Results: Ventricular unloading resulted in a significant decrease in both myocardial BNP expression (Pre VAD 4.17 ± 0.44 vs. Post VAD 4.13 ± 3.97, p = 0.031) as well as fibrosis (Pre VAD 1.71 ± 0.76 vs. Post VAD 1.14 ± 0.69, p = 0.03). Regression analysis demonstrated an inverse correlation between TGF-B expression in COL IA2. BNP and COL IA2 (R = 0.99, p < 0.001), BNP and COL IA2 (R = 0.99, p < 0.001), and TGF-B and COL IA2 (R = 0.99, p < 0.001).

Conclusions: Ventricular unloading with VAD reduces myocardial BNP, TGF-B, and collagen expression in association with histologic regression of fibrosis.

Mechanical Circulatory Support: An 18-Year Experience With Over 460 Patient Years of Support

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Background: Mechanical circulatory support (MCS) devices have evolved from a primarily resuscitative measure to a viable treatment for end-stage heart failure patients. An 18-year clinical experience representing over 460 patient years of support from a single device (Novacor LVAS) was retrospectively reviewed. Methods: Utilizing data from the international registry, patient database, and manufacturer database, patient outcomes were analyzed for 197 patients at over 90 international centers. Results: The mean age at time of implant was 43 years (12-78 years). Etiology was non-ischemic cardiomyopathy in 776 (57%), ischemic cardiomyopathy 403 (30%), acute myocardial infarction in 54 (4%) and other cardiovascular conditions (post-cardiomyopathy, myocarditis, etc.) in 92 (7%). The intent to treat was as a bridge to transplantation in 93% of patients, as a bridge to recovery in 4% and as a "Destination Therapy" in 3%. Currently, 70% of these patients are supported, 706 patients survived to transplantation, and 26 patients were weaned from the device following myocardial recovery. The mean support duration was 129 days (0 - 1613 days), and over 460 years of patient support has been accumulated. There were no patient deaths due to device failure and after the initial high risk period post-implant (first 3 months), 70.75% of patients achieved a favorable outcome (i.e. transplantation or weaning). The majority of long-term recipients (85% of those supported >30 days) were able to be discharged from hospital and return to near normal life activities. Conclusions: 1) This substantial experience has demonstrated MCS can provide an effective therapeutic option for end-stage heart failure. 2) Enhanced quality of life has been demonstrated with patients discharged from hospital and able to return to normal daily activities. 3) Overall device safety has been demonstrated with no patient deaths due to device failure, and 4) Long-term device durability has been demonstrated with patients supported for over 4 years on a single device. The findings support continued use of MCS, both for short-term use as a bridge to transplant and long-term support as a potential "destination therapy".

Reduced Myocardial Blood Flow During Left Ventricular Assist Device Support May Lead to Premature Closure of Coronary Artery Bypass Grafts

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Background: Patients who fail to wean from cardiopulmonary bypass following cardiac surgery can be supported hemodynamically with a left ventricular assist device (LVAD). Because LVAD support results in profound pressure and volume unloading of the left ventricle, we sought to determine what effect this reduction in workload would have on myocardial oxygen consumption (MVO2), myocardial blood flow (MBF) and bypass graft patency.

Methods: Positron emission tomography (PET) scanning was performed in 9 LVAD patients (age 57±14 years) with no ischemic cardiomyopathy (DCM) and 12 normal subjects, using C-11 acetate to measure MVO2 and N-13 ammonia to measure MBF. Five other patients (age 56±12 years) with coronary disease (CAD), who underwent coronary artery bypass grafting (CABG) and required LVAD implantation for post-cardiotomy shock (with patent grafts), had coronary angiography performed during support device.

Results: PET scanning in the DCM patients was performed 65±29 days following LVAD implantation and revealed a significant reduction in both MVO2 (0.03±0.01 vs. 0.05±0.01 ml/min.l; p<0.001) and MBF (0.49±0.15 vs. 0.56±0.17 ml/min.l; p<0.03) compared to normal subjects. Coronary angiography in the CAD patients was performed 115±126 days after CABG and LVAD implantation. Twelve of the 16 bypass grafts (75%) were either totally occluded or significantly narrowed.

Conclusions: In a cohort of patients with DCM, LVAD support reduced both MVO2 and MBF. Autoregulatory mechanisms that match MBF with MVO2 may explain the observed downward regulation in blood flow that followed left ventricular unloading. Low MBF may be implicated in the premature graft failure observed in our CABG patient population and may negatively impact the potential for myocardial recovery and device weaning in this population.