ABSTRACTS

Oral presentations on Friday, January 12th
7:00 – 8:15 am

1. **JB Durand** - University of Texas, MD Anderson Cancer Center, Baylor College of Medicine - The Use of Contractile Reserve Dobutamine Echocardiography for Recovery Prediction in Chemotherapy Associated Cardiomyopathy

2. **Nir Uriel** - University of Chicago - Significant Reverse Remodeling Following Ambulatory IABP Implantation

3. **Katarzyna Hryniewicz** - Minneapolis Heart Institute / Abbott Northwestern Hospital - Two Year Outcomes in Patients Successfully Explanted from Durable Left Ventricular Assist Device Support.

4. **Sara Kalantari** - University of Chicago - REMODEL: Reverse Remodeling Effects of Valsartan/Sacubitril (Entresto)


6. **Iosif Taleb** - U of Utah - Feasibility and Effectiveness of a Shock Team Approach in Refractory Cardiogenic Shock: Preliminary Results

7. **Stavros Stavrakis** - University of Oklahoma Health Sciences Center - Transcutaneous vagus nerve stimulation attenuates cardiac remodeling in a rat model of heart failure with preserved ejection fraction

8. **Stephen M Ratchford** – U of Utah - Cardiovascular Responses to Dynamic Handgrip Exercise in Patients with Heart Failure with Preserved Ejection Fraction

9. **Miguel Alvarez Villela** - Montefiore Medical Center/Albert Einstein College of Medicine - High-Intensity Interval Training in Patients With Left Ventricular Assist Device

Poster Session during lunch on Thursday & Friday, January 11 -12th
The Use of Contractile Reserve Dobutamine Echocardiography for Recovery Prediction in Chemotherapy Associated Cardiomyopathy

JB Durand, MD, University of Texas, MD Anderson Cancer Center, Baylor College of Medicine

Introduction: Myocardial viability is dependent on imaging evidence of myocardial functional reversibility. A variety of imaging modalities can analyze tissue viability and are used as a method to predict tissue recovery in patients with heart failure, but there is limited data and agreement on which modality is a better predictor of viability and recovery potential in cancer patients with newly diagnosed left ventricular systolic dysfunction (LVSD). Our previous analysis has demonstrated lower mortality outcomes in cancer patients with full recovery of LV systolic function. We predict that dobutamine stress echocardiography will be a measure viability and functional recovery potential in patients with new LVSD.

Methods: We performed a prospective case assessment on cancer patients with new LVSD (LVEF < 50%). Based on inclusion and exclusion criteria, a total of 26 subjects were enrolled. The patients underwent dobutamine echocardiogram (intravenous doses 2.5 mcg, 5 mcg, 10 mcg) to evaluate dobutamine response. Complete recovery was defined as an increase in left ventricular ejection fraction (LVEF) of more than 10 absolute percent points and achieving an LVEF of more or equal to 50%. Partial recovery was defined as an increase in 10 absolute percent points but not achieving at least an LVEF of 50%. No recovery was defined as lack of increase in LVEF or an increase lower than 10 absolute percent points. Data was analyzed to assess the ability of dobutamine echocardiography in predicting recovery of LV systolic function.

Results: Out of twenty-six patients, 19 patients (mean age 58 (19 - 85) years, 12 female) had echocardiographic evidence of augmentation with dobutamine (p-value 0.28). Twenty-six percent (n = 5) of these patient’s showed full recovery. Twenty-six percent (n = 5) had a partial response and 48% (n = 9) showed no recovery. Seven patients (mean age 62 years, 7 female) had no echocardiographic evidence of augmentation with dobutamine. Of these 7 patients, none showed full recovery, 43% (n = 3) showed partial recovery and 57% (n = 4) showed no recover. Conclusions: The major finding from our small cohort of patients revealed that in cancer patients with new LVSD and lack of augmentation with dobutamine may suggest a dismal opportunity for complete LV systolic function recovery. Our sample size is a significant limitation to show the potential predictive capability that this technique may have. Larger studies are needed to examine the potential of dobutamine echocardiography in predicting functional recovery and outcomes in this population.

Significant Reverse Remodeling Following Ambulatory IABP Implantation

Nir Uriel, MD, University of Chicago, Chicago, IL

Teruhiko Imamura*, MD, PhD1), Colleen Juricek*, RN,2) Ann Nguyen, MD,1) Ben Chung, MD,1) Daniel Rodgers, BA,1) Gabriel Sayer, MD,3) Nitasha Sarwat, MD,1) Gene Kim, MD,1) Jayant Raikhelkar, MD,1) Takeyoshi Ota, MD, PhD,2) Tae Song, MD,2) Daniel Burkhoff, MD, PhD,3) Valluvan Jeevanandam, MD,2) and Nir Uriel, MD, MSc1)

Purpose:The NuPluse CV intravascular ventricular assist system (iVAS) is an ambulatory Intra Aortic Balloon Pump (IABP) that allows for subacute or chronic cardiac support. The pump consists of a durable IABP placed through subclavian artery access, and a transcutaneous electromechanical conduit for air and electrocardiographic data transmission. The aim of this study was to report the effect of iVAS on ventricular reverse remodeling.

Methods:All patients with advanced heart failure received iVAS implantation as a bridge to transplantation or a bridge to candidacy since April 2016 as part of the iVAS feasibility study. Transthoracic echocardiography was performed just before implantation and again at 30 days or just prior to explantation, whichever came first were compared.

Results:18 patients (58.8 ± 7.4 years old, 15 males, 50% ischemic cardiomyopathy) were enrolled. The duration of iVAS support averaged 53 ± 43 days. 14 patients were bridged to cardiac replacement therapy after 35 ± 19 days and the remaining 4 patients have been supported for 118 ± 41 days. There were no deaths during iVAS support. At 30 days, there was a significant improvement in LVEF (16.53 ± 11.91 vs 24.43 ± 12.79; p=0.007), marked reduction in LA size (62.74 ± 35.72 vs 33.77 ± 17.20; p<0.001) and a reduction in mitral regurgitation severity (1.8 ± 1.4 vs 1.2 ± 1.2; p=0.03) (Table 1A). Right ventricular function improved dramatically (25.35 ± 12.91 vs 42.05 ± 12.43; p<0.001) and both right ventricle and
trial size decreased in size (p=0.04 and 0.01, respectively), tricuspid annular plane systolic excursion and velocity of tricuspid annular systolic motion, improved significantly (p<0.05 for all comparisons; Table 1B).

Conclusion: Reverse remodeling of both the LV and RV was observed following 30 days of iVAS support. Further studies should examine the use of this technology as a bridge to recovery.

### Table 1B: LV and RV Measures before and during iVAS support

<table>
<thead>
<tr>
<th>Measure</th>
<th>Before iVAS</th>
<th>During iVAS</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. Left ventricle</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEDD, cm</td>
<td>7.13 ± 1.27</td>
<td>6.45 ± 1.46</td>
<td>0.059</td>
</tr>
<tr>
<td>LVMI, g/m²</td>
<td>120.03 ± 35.13</td>
<td>103.81 ± 32.19</td>
<td>0.16</td>
</tr>
<tr>
<td>LAVI, mL/m²</td>
<td>62.74 ± 35.72</td>
<td>33.77 ± 17.20</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>16.53 ± 11.91</td>
<td>24.43 ± 12.79</td>
<td>0.007*</td>
</tr>
<tr>
<td>E/e' ratio</td>
<td>20.97 ± 7.94</td>
<td>14.01 ± 5.53</td>
<td>0.009*</td>
</tr>
<tr>
<td>AR, grade</td>
<td>0.5 ± 0.7</td>
<td>0.3 ± 0.5</td>
<td>0.10</td>
</tr>
<tr>
<td>MR, grade</td>
<td>1.8 ± 1.4</td>
<td>1.2 ± 1.2</td>
<td>0.030*</td>
</tr>
<tr>
<td><strong>B. Right ventricle</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RVEDA, cm²</td>
<td>23.31 ± 8.51</td>
<td>19.59 ± 5.61</td>
<td>0.039*</td>
</tr>
<tr>
<td>RA area, cm²</td>
<td>20.12 ± 5.71</td>
<td>14.83 ± 6.39</td>
<td>0.014*</td>
</tr>
<tr>
<td>RVFAC, %</td>
<td>25.35 ± 12.91</td>
<td>42.05 ± 12.43</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>TAPSE, cm</td>
<td>1.48 ± 0.51</td>
<td>1.77 ± 0.52</td>
<td>0.008*</td>
</tr>
<tr>
<td>TV S', cm/s</td>
<td>8.96 ± 2.62</td>
<td>10.39 ± 3.22</td>
<td>0.047*</td>
</tr>
<tr>
<td>TR, grade</td>
<td>0.8 ± 0.9</td>
<td>0.8 ± 0.7</td>
<td>0.82</td>
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</table>

LVEDD, left ventricular end-diastolic diameter; LVMI, left ventricular mass index; LAVI, left atrial volume index; LVEF, left ventricular ejection fraction; E/e’ ratio; the ratio of mitral peak velocity of early filling to early diastolic mitral annular velocity; AR, aortic valve regurgitation; MR, mitral valve regurgitation; RVEDA, right ventricular end-diastolic area; RA, right atrial; RVFAC, right ventricular fractional area change; RV S’, velocity of tricuspid annular systolic motion; TR, tricuspid valve regurgitation.

N = 18 except for E/e’ ratio (N = 14)
*p <0.05 by paired t-test

### Two Year Outcomes in Patients Successfully Explanted from Durable Left Ventricular Assist Device Support.

Benjamin Sun, MD, FACS, Minneapolis Heart Institute / Abbott Northwestern Hospital

Katarzyna Hryniewicz, Carrie Weaver, Michael Samara, Karol Mudy, Benjamin Sun.

Purpose: Myocardial recovery in patients (pts) supported with left ventricular assist devices (LVAD) is rare. Long term outcomes of pts who had durable LVAD explanted is also unknown. We report 2 year outcomes of LVAD pts at our institution who demonstrated myocardial recovery and had their LVAD explanted between 2011 and 2015.

Methods: A weaning protocol was developed for LVAD pts, who improved LV EF to ≥ 40%. This included at least 6 months of guideline directed optimal heart failure (HF) therapy on stable LVAD speed with consistent mean arterial pressures of 60-80 mmHg, no hospitalizations for at least 3 months, evaluation of LVEF with serial echocardiograms and MUGA scan, cardiopulmonary stress testing (CPST), and right heart catheterization. In addition pts underwent CPST at 6000 RPMs while on IV anticoagulation with a pulmonary artery catheter in place. LVAD explantation was carried out predominantly through a full sternotomy with all components removed. After explantation pts were maintained on HF therapy and followed in the HF clinic.

Results: During the study period LVAD explantation was performed in 12 pts, mean age 44, 85% males, mean INTERMACS profile 1.8, with 46% of pts being INTERMACS 1. Mean LVEF pre-LVAD was 13%. Etiology of cardiomyopathy was ischemic in 3 pts and non-ischemic in 9. Mean duration on LVAD support was 752 days (182-1358). Ten out of 12 pts were alive at 2 years. One pt was lost to followup and one died from a ruptured abdominal aorta after weight lifting at day 358. One pt underwent heart transplantation and another required LVAD reimplantation at 6 months. 8 pts are maintained on medical therapy and remain NYHA Class I or II, mean LVEF of 40% (20%-50%) and VO2 Max 16.7-32ml/kg/min.

Conclusion: In our study LVAD explantation after myocardial recovery showed good and durable outcomes out to two years with respect to LVAD free survival, left ventricular systolic function and functional status. Interestingly, recovery to explant was seen after longer LVAD support time than others have reported. This may be due to rigid selection criteria for those offered explantation in our practice as well as allowing adequate time for myocardial recovery. Further studies
may be helpful in identifying optimal length of time on LVAD support to allow for the chance of myocardial recovery as well as durability of recovery beyond 2 years.

REMODEL: Reverse Remodeling Effects of Entresto (valsartan/sacubitril)
Sara Kalantari, MD, University of Chicago, Chicago, IL

Background: Valsartan/sacubitril, an angiotensin receptor-neprilysin inhibitor, significantly reduced the rates of death from any cause and from cardiovascular causes as well as the rates of hospitalizations for worsening heart failure as compared to a target-dose enalapril-based regimen for patients with HFrEF. The pathophysiology underlying the benefit of valsartan/sacubitril and its effects on remodeling remain unknown. Here we seek to further elucidate the benefits of valsartan/sacubitril on ventricular remodeling and functional status.

Methods: In this prospective, single-arm longitudinal study, 40 patients were initiated on valsartan/sacubitril after a two week run in period of ACE or ARB alone. The primary end-point was the degree of reverse remodeling (change in LV and RV size, volume, shape, and function) as assessed by 3D-TTE with surface analysis at 3 months compared to baseline using paired t-tests. Secondary endpoints were peak VO2 and 6-minute walk distance.

Results: Interim analysis of 24 patients shows significant reduction in LV and RV volumes with improvement in LV conicity and sphericity indices at 3 months. Interim analysis revealed improved 6-minute walk distance (440 ± 97 vs 466 ± 98 m; p = 0.007) and no change in peak VO2 (18.5 ± 5.4 vs 18.8 ± 4.7; p = 0.56) at 3 months.

Conclusion: This is the first study to investigate the effects valsartan/sacubitril on ventricular remodeling and functional status at 3 months. Interim analysis suggests improved remodeling.

Myocardial Recovery after Extracorporeal Cardiopulmonary Resuscitation: A pilot analysis
Joseph Tonna, MD, University of Utah, Salt Lake City, UT

Background: The use of extracorporeal life support therapies for acute cardiopulmonary failure has recently expanded in use throughout the world. Though randomized controlled trials of extracorporeal cardiopulmonary resuscitation (eCPR) on patients with acute refractory cardiac arrest are lacking, there is a plausible physiologic benefit to eCPR in cases of refractory myocardial ischemia. Compared to conventional closed chest compressions, eCPR may provide increased myocardial perfusion during the first hours to days after cardiac arrest. While it is difficult to dynamically monitor myocardial ischemia/perfusion during and after cardiac arrest, we sought to examine the change in cardiac ejection fraction between cardiac arrest patients treated with and without eCPR.

Methods: Out of hospital cardiac arrest cases from Salt Lake City, UT were analyzed from 7/2008 through 10/2017 and merged cases of extracorporeal cardiopulmonary resuscitation at the University of Utah. Cases were analyzed by eCPR use, presence of two sequential echocardiograms during the index admission, and survival. Descriptive statistics, including mean (SD) and median (interquartile range) were used to assess patient characteristics. Categorical characteristics were compared using chi-square test or Fisher exact test. Continuous characteristics were compared using independent samples t-test or Wilcoxon-Mann-Whitney test. 95% confidence intervals (CIs) and p-values were reported from all comparisons. Statistical analyses were conducted in STATA 15. Significance was assessed at the 0.05 level and all tests were two-tailed.

Results: 1,106 cases of adult out of hospital cardiac arrest were identified since 7/2008. The average age was 59 (SD 19.2) years old with 67% male. 50% of the arrests were witnessed, and the initial arrest cardiac rhythm was 39% asystole, and 20% ventricular fibrillation (VF). 111 patients had at least one echocardiogram, and 25 had two or more. Since mid-2015, eCPR was successfully used in 15 cases. Patients placed on eCPR were more likely to have an initial cardiac rhythm of ventricular fibrillation (VF) or ventricular tachycardia (VT). Among all patients, the initial ejection fraction was worse among patients who received eCPR (p=0.0015), which retained significance among survivors (p=0.01). Despite this, eCPR patients were more likely to have improved ejection fraction on a second echocardiogram.
compared to conventional CPR treated patients (p<0.001), including among survivors (n=140, p<0.001), though many patients did not have second echocardiograms. Isolated to patients who had two sequential echocardiograms (n=25), this lost significance (p=0.07).

Conclusions: This pilot analysis suggests that echocardiographic measurement of ejection fraction is feasible in cardiac arrest patients treated with extracorporeal cardiopulmonary resuscitation, and that despite a worse initial ejection fraction, these patients have large improvements in ejection fraction compared to patients treated with conventional cardiopulmonary resuscitation. Studies are needed to evaluate the role of eCPR for myocardial recovery after cardiac arrest.

Acknowledgements: This investigation was supported by the University of Utah Population Health Research (PHR) Foundation, with funding in part from the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant 5UL1TR001067-05 (formerly 8UL1TR000105 and UL1RR025764).

Feasibility and Effectiveness of a Shock Team Approach in Refractory Cardiogenic Shock: Preliminary Results
Iosif Taleb, MD University of Utah, Salt Lake City, UT

Background: Despite efforts to improve treatment of refractory cardiogenic shock (rCS), prognosis has remained poor. Multidisciplinary “Shock Teams” have been proposed as a strategy to streamline care delivery and improve outcomes. However, the feasibility and efficacy of this strategy has not yet been explored.

Methods: Our institution’s “Shock Team” was established in Apr 2015 and consists of a heart failure (HF) cardiologist, an interventional cardiologist and a HF surgeon. Between Apr 2015- Dec 2016 forty consecutive patients were enrolled since program initiation (“Shock-team” cohort) and compared with the immediately preceding 40 patients (“Control” cohort). All of the patients had rCS based on predefined criteria and required Mechanical Circulatory Support (MCS) support. Primary and secondary outcomes were 30-day mortality and “Shock to Support” time, respectively.

Results: More patients from the “Shock Team” cohort had at presentation shock liver (p=0.01), acute renal failure (p=0.04), lower ejection fraction (p=0.05), higher right atrial pressure (p=0.04) and underwent cardiopulmonary resuscitation (p=0.05). Despite a sicker population comprising the “Shock Team”, the primary outcome of 30-day mortality did not show statistical significant difference in a Cox regression model and it was numerically lower in shock team (35% Vs 47.5%; p=0.25). Correspondingly, “Shock to Support” time revealed faster MCS utilization on “Shock Team” (9±30 Vs 16±28 hrs., p=0.21).

Conclusion: A multidisciplinary “Shock Team” approach deemed feasible and aside from not delaying implementation of MCS, decision making was more comprehensive and guideline driven. Even though rCS at presentation, in the “Shock Team” cohort, was more severe, 30-day mortality was numerically lower. These encouraging findings warrant validation by prospective large-scale randomized trials.

Transcutaneous vagus nerve stimulation attenuates cardiac remodeling in a rat model of heart failure with preserved ejection fraction
Stavros Stavrakis, MD, University of Oklahoma Health Sciences Center

Liping Zhou, Adrian Filiberti, Christian Fleming, Mary Beth Humphrey, Benjamin Scherlag, Sunny Po, Stavros Stavrakis

Background: Heart failure with preserved ejection fraction (HFpEF) has become a major public health concern and, so far, no treatment has been shown to decrease morbidity or mortality. Recent animal and human studies support the notion that proinflammatory and profibrotic stimuli play a central role in the development of HFpEF. We have previously shown that transcutaneous vagus nerve stimulation (tVNS) is anti-inflammatory. We examined the effects of short-term intermittent tVNS on cardiac function, inflammation and fibrosis in a rat model of HFpEF.

Methods: Forty-eight Dahl salt-sensitive (DS) rats were randomized to 3 groups: low salt (0.3% NaCl; n=12) and high salt (8% NaCl) with either active tVNS (n=18) or sham tVNS (n=18) starting at 7 weeks of age. After 6 weeks of either low or high salt diet, sham or active tVNS was implemented for 30 minutes daily for 4 weeks. tVNS (20Hz, 0.2ms, 3mA) was accomplished by placing two oppositely charged magnetic electrodes over the auricular concha region, inside and outside, respectively, at each ear. In the sham tVNS group, the electrodes were placed on the auricular margin, which is devoid of
vagus innervation. Echocardiography was performed at baseline and 4 weeks after treatment (endpoint) to assess cardiac function. Blood was collected at the same time points for cytokine analysis. Animals were euthanized at the end of the experiment and the left ventricle was examined for fibrosis.

Results: After 6 weeks of high salt diet, rats developed hypertension and left ventricular hypertrophy compared to low salt rats (129.4±14.6 mmHg vs. 114.1±17.4 mmHg ; p=0.03 and 2.3±0.2 mm vs. 2.0±0.1 mm; p=0.001, respectively). tVNS attenuated the increase in blood pressure after 4 weeks of treatment (124.1±5.2 mmHg vs. 158.0±5.0; p=0.001). In addition, tVNS prevented the deterioration of diastolic function compared to sham stimulation (E/A ratio: 1.4±0.1 vs. 1.6±0.1, p=0.005; E/e’ ratio: 8.1±0.5 vs. 11.1±0.5, p=0.001) and improved circumferential strain (-24.1±1.0% vs. -19.7±1.0%, p=0.002), without a change in left ventricular ejection fraction. Serum cytokines were not elevated in either group. Left ventricular fibrosis was decreased in the tVNS group compared to the sham group (2.5±1.2% vs. 4.1±2.2%, p=0.02) to the levels seen in the low salt rats (2.3±1.5%).

Conclusion: These data indicate that tVNS ameliorates diastolic dysfunction and prevents cardiac remodeling in hypertensive rats, suggesting that such a treatment may be used chronically to improve diastolic function in patients with HFpEF. Further studies to examine the efficacy of this novel treatment in patients with HFpEF are warranted.

Cardiovascular Responses to Dynamic Handgrip Exercise in Patients with Heart Failure with Preserved Ejection Fraction

Stephen M Ratchford, MD, University of Utah, Salt Lake City, UT

Heather L. Clifton1,2, D. Taylor La Salle3, Ryan M. Broxterman1,2, Joshua F. Lee1,2, John J. Ryan4, Russell S. Richardson1,2,3, Joel D. Trinity1,2,3, and D. Walter Wray1,2,3

Background: Heart failure with preserved ejection fraction (HFpEF) is associated with symptoms of exercise intolerance, which may correspond to disease-related changes in the peripheral circulation. A small muscle mass (dynamic handgrip, HG) exercise that evokes minimal cardiopulmonary stress was utilized to concomitantly evaluate exercising muscle blood flow and conduit vessel endothelium-dependent vasodilation in patients with HFpEF compared to hypertensive controls (CON).

Methods: We evaluated heart rate (HR), stroke volume (SV), cardiac output (CO), mean arterial pressure (MAP), and brachial artery blood velocity and diameter in CON (n = 25, 52 ± 7 y, BMI 30 ± 6 kg/m2) and patients with HFpEF (n = 25, 69 ± 10 y, BMI 33 ± 6 kg/m2) during dynamic HG exercise (15, 30, and 45% MVC, 1 contraction/sec). Brachial artery blood flow and vascular conductance were determined to quantify the hemodynamic response to HG exercise, and changes in brachial artery diameter were evaluated to assess conduit vessel vasodilatory capacity.

Results: While HR modestly increased in both groups at 45% MVC (10 ± 2 and 8 ± 2 bpm compared to rest, HFpEF and Control), SV and CO were unchanged across exercise intensities in both groups. Brachial artery blood flow was similar between groups at the lowest exercise intensity (15% MVC: 145 ± 41 vs. 158 ± 17 ml/min, HFpEF vs. CON) but was blunted by 20-40% in HFpEF patients at higher work rates (30% MVC: 229 ± 8 vs. 274 ± 23 ml/min, 45% MVC: 283 ± 17 vs. 399 ± 34 ml/min, HFpEF vs. CON). Brachial artery vascular conductance increased to a similar degree in both groups at 15 and 30% MVC, but was blunted by ~20% at the highest exercise intensity (45% MVC: 2.74 ± 0.21 vs. 3.54 ± 0.30 ml/min/mmHg, HFpEF vs. CON). Brachial artery shear rate was similar between HFpEF and CON at all exercise intensities. Brachial artery diameter increased across work rates in both HFpEF (15% MVC: 3 ± 1%, 30% MVC: 6 ± 1%, 45% MVC: 8 ± 1%) and CON (15% MVC: 2 ± 1%, 30% MVC: 4 ± 1%, 45% MVC: 7 ± 1%), and there was no difference between groups.

Conclusions: These results provide evidence for impaired skeletal muscle blood flow during small muscle mass exercise in patients with HFpEF that cannot be attributed to a disease-related alteration in central hemodynamics. However, brachial artery vasodilation in response to the step-wise, sustained shear stimulus evoked during exercise was similar between groups, suggesting a preservation of endothelium-dependent dilation in patients with HFpEF compared to their hypertensive counterparts. Together, these findings suggest an overall derangement in the regulation of muscle blood flow during exercise in patients with HFpEF that is not attributable to disease-related changes in endothelial function.
High Intensity Interval Training in Patients with Left Ventricular Assist Device
Miguel Alvarez Villela, MD, Montefiore Medical Center/Albert Einstein College of Medicine

Miguel Alvarez Villela, Thiru Chinnadurai, Kalil Salkey, Andrea Furlani, Julia Shin, Ileana Pina, Ulrich Jorde, Snehal Patel

Background
High-intensity interval training (HIIT) is safe and efficient in patients with heart failure and reduced ejection fraction (HFrEF). One study showed that a supervised HIIT program in these patients could lead to significant improvements in exercise capacity and to left ventricular (LV) reverse remodeling. Severe exercise limitation persists after LVAD implantation in patients with advanced HFrEF. Whether HIIT can improve aerobic capacity, functional status and LV function these patients is unknown.

Methods
We examined the effects of an individualized HIIT program in patients with LVAD (HeartMate II) support. After 2 cycle ergometer based cardiopulmonary exercise tests (CPX), test with best effort taken as true baseline, 15 supervised training sessions (TS) were prescribed. TS were individualized using baseline CPX data and lasted 30 min. each: Three min. warm-up (50% of peak power output (PPO)), and six 30 sec. challenges (100% of PPO) with six 4 min. recovery periods (40% of PPO). Lower intensity was allowed in the first 3 and in any other poorly tolerated sessions. CPX was repeated after training. Two blinded independent readers identified oxygen consumption (VO2) at ventilatory threshold (VT) and peak exercise (pVO2) in all tests. An echocardiogram guided “turn-down” study (pump speed reduced to 6,000 rpm) was performed in each patient before and after training. LV size and systolic function were assessed by a reader unaware of the study intervention. A Kansas City Cardiomyopathy Questionnaire (KCCQ) was administered before and after training.

Results
Nine subjects were enrolled (6 male, 7 NICM) with median age 53yrs (range: 29-71) and LVAD duration 28 months (10-31). One patient did not complete training due to drive line malfunction and one voluntarily withdrew. Overall adherence to training was good, a median (25th-75th percentile) of 87% (87-100%) of sessions and 86% (76-99%) of prescribed workload (watts) were completed. No serious adverse events occurred. Training intensity was high. Achieved percentage of heart rate reserve was 82% (69-99%) during challenges and 66% (55-74%) during recovery periods. The rate of perceived exertion during challenges was 14 (12-15) on Borg Scale 6-20. Seven patients underwent repeat CPX. HIIT significantly improved pVO2 (mean±SD, 11.7±2.5 to 12.3±2.4 ml.kg.min-1; p=0.02) and VO2 at VT (7.0±1.3 to 9.3±1.4 ml.kg.min-1; p=0.01) but not peak ventilatory efficiency (VE/VCO2: 42±7 to 41±6; p=0.3). Heart rate at VT and peak exercise did not change significantly after training (96±20 to 102±16; p=0.7 and 123±28 to 118±23; p=0.4, respectively). “Turn-down” echocardiograms did not show a change in LV size (LVEDV 186±79ml vs. 180±93; p=0.4) or function (LVEF 29±8% vs. 29±7%; p=0.9) at lowered speed. After training, the median change (25th-75th percentile) in KCCQ score was +3.2 (-3.2 - +12.1; p=0.3) in the overall summary scale, and +6.25 (+3.7 – +17.7; p=0.03) in the physical limitation subscale.

Conclusions
CPX guided HIIT is safe and highly efficacious in improving exercise capacity and symptoms of physical limitation in patients with LVAD. With no change in intrinsic LV function or heart rate response during exercise, the observed improvement in aerobic capacity seems owed to increased peripheral oxygen extraction. These findings deserve further exploration.
Versatile potential of a new rotary blood pump HeartMate 3 in patients with multiple assist device thrombosis
Jens Garbade, MD, Heart Center Leipzig - Leipzig Germany

Objectives: The rotary blood pump HeartMate 3 (HM 3) from Thoratec® is a left ventricular assist device which received the CE mark recently. So far first results of the multicenter clinical trial show promising data. None of the patients developed a pump thrombosis. The aim of the study was to analyse high-risk patients after LVAD exchange with a HeartMate 3.

Methods: Between 1/2016 and 8/2017, 7 of 50 patients with HM3 implantation were a pump exchange due to pump thrombosis in an HVAD (n=4) or a HM II (n=3). Patients developed a pump thrombosis in the initial LVAD after 953±651 days and had already multiple lysis or previous pump exchange. The procedure was performed via re-sternotomy. The mean age of the 7 male patients was 50±20 years. An ischemic cardiomyopathy was diagnosed in 50% of the patients. Results: Mean follow up was 283±49 days. All patients are discharged and alive. A pump thrombosis, hemolysis or stroke were not observed in the follow up period. Three patients needed a right ventricular assist device intra-operatively (Levitronix), one patient was able to wean from RVAD and the other one was transplanted after 92 days. Two patients needed a re-exploration due to bleeding.

Conclusion: An upgrade to HM 3 after pump thrombosis shows an excellent 6 month survival. All patients received the 6 months follow up without any signs of a re-thrombosis of the new pump, therefore this pump seems to be optimal in risk patients.

Croatian ECMO Network: SPOKE – hub Paradigm
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Mate Petricevic MD, Ph.D. ; Hrvoje Gasparovic MD, Ph.D. ; Bojan Biocina MD, Ph.D.

Extracorporeal membrane oxygenation (ECMO) represents a therapeutic option in patients with refractory cardiogenic shock and terminal respiratory failure. This strategy is limited to a restricted number of centers with capabilities for implanting ECMO, and in some degree capabilities for managing patients while on this support. Herein, we report on the experience of Croatian national ECMO programme. The very first ECMO procedure has been performed back in 1987 at University Hospital Center Zagreb, Department of Cardiac Surgery. The patient underwent post cardiotomy ECMO (SciMed Kolobow type membrane oxygenator + Medtronic Biomedicus pump) and was successfully weaned of support shortly after. Mechanical circulatory support programme was terminated in 1995 and re-established in 2008. Development of ECMO support programme paralleled short and long-term mechanical circulatory support programme development. Following successful initial experience with ECMO support at the University Hospital Centre Zagreb, the ECMO programme has gradually spread to other secondary and tertiary care centers in Croatia. Croatian national ECMO network was established in 2013 and is grounded on spoke-hub principle. There is one national respiratory ECMO hub (Department of Infectious Diseases Zagreb) and 5 circulatory ECMO hubs (university hospitals with cardiac surgery service available (University Hospital Centre (UHC) Zagreb, University Hospital Dubrava, UHC Rijeka, UHC Split and UHC Osijek). Speaking of spoke-hub principle, all hospitals with cath labs and some district hospitals without ones are considered as spokes. The major difference between the respiratory and circulatory ECMO is that there is usually enough time to transport patient with respiratory failure to the “respiratory ECMO hub” center whereas this is not the case in “circulatory ECMO” where the support should be applied locally as soon as possible and patient should be transported while on support to the center of the final treatment. This explains why we have only one “respiratory ECMO hub”. In general, 32 ECMO consoles are utilized in Croatian ECMO network. Two types of ECMO consoles are in use. Whereas VA ECMO Hubs use “in-hospital” transportable consoles (Maquet PLS), spoke centers use transportable consoles (Maquet Cardiohelp). Both types of consoles are used in national respiratory ECMO hub. In the period between
2013 and March 2017, Croatian ECMO network yielded 688 ECMO procedures. Of those, 315 (mostly VA) were performed at UHC Zagreb, 190 (mostly VV) at Department of Infectious Diseases Zagreb, 77 (mostly VA) at University Hospital Dubrava, 46 procedures (mixed VA and VV) at UHC Rijeka, 23 procedures at UHC Split, 12 at UNC Osijek and 25 procedures in other spokes, respectively. When analyzing the distribution of procedures between hubs and spokes, the skewed distribution is present with only 25 out of 693 procedures being performed in “Tier One” centers. ECMO programme is being developed in Croatia and has evolved from extended cardiopulmonary bypass to “eCPR—cardiopulmonary resuscitation”. The technology (equipment and operative techniques) has been disseminated over the hub-spoke network and theoretically, we may say that coverage is complete. However, the network is underutilized by regional centers (spokes) with challenges not limited just to logistical ones. Apart from asymmetrical technique adoption, we may conclude that ECMO network in Croatia has been set up with 693 procedures being performed so far. There is a room for improvement, in particular, asymmetrical technique adoption with underutilization of network in regional centers should be addressed in future keeping in mind that challenges to further growth of the network are not limited to logistical ones. Multidisciplinary approach is needed to educate medical practitioners in Croatia and increase awareness on the importance of such a technology. Even though we may often hear: “Easier said than done”, the crucial step to address the underutilization in regional centers (spokes) would be putting the plan in action. This is particularly important for VA ECMO programme as VV ECMO support is usually not emergent and patients may be transported to the VV Hub, whereas that is not the case in VA ECMO where cardiogenic shock prompts immediate attention and support. VA ECMO is lifesaving procedure and as the timing of implantation is crucial, its spread should go to “as wide as possible” level of the national healthcare system providing equal chances of surviving cardiorespiratory arrest throughout the whole territory of the Republic of Croatia. A total number of 693 procedures being performed so far with a 30-day survival rate of 47% makes us proud but not content as there is still room space for improvement, in particular in spoke centers where the network is being underutilized so far.

VAD Program in the Republic of Kazakhstan
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Objective: The objective of this study was to determine outcomes of patients with left ventricular assist devices (LVAD) in a country with a restricted heart transplantation (HTx) program.

Methods: The Center established the sole ventricular assist device (VAD) program in Kazakhstan in 2011 before the beginning of the HTx program providing VAD support to all regions of this, the world’s 9th largest country. From November 2011 to October 2017, 238 patients underwent implantation of 249 VAD at our Center. 231 LVAD patients received HeartMate II (n=97, 42%), HeartWare (n=54, 23%) and HeartMate 3 devices (n=80, 35%). Mean age was 50 ± 13 years old (9 - 76), idiopathic cardiomyopathy was in 103 patients (44%), ischemic cardiomyopathy - in 93 patients (39%).

Results: In 146 patients (62%) VAD is used as BTT and in 92 (38%) as DT, but only 25 (10.6%) patients were transplanted. Kaplan-Meier survival estimates for patients who continued on LVAD support after 1 year were 81.6% in HeatMate II group, 77.7% - HeartWare, 90.6% - HeartMate 3, after 2 years survival rates were 63.2%, 52.1% and 85% accordingly. Before 30 days after implantation of LVAD right ventricular failure (n=63, 26.9%) and bleeding requiring surgery (n=21, 9%) were the most common adverse events. After 30 days driveline infections (n=81, 34.6%) and strokes (n=53, 22.6%) were the most common complications. There were no pump thrombosis and hemolysis in HeartMate 3 patients group. Our patients are discharged home to regions that distant from our Center up to 2000 km. While at home, patients communicate health status, driveline status, weekly INR results directly to the VAD coordinator and nurses using a software application for mobile phone devices.

Conclusions: VAD program in our country was the trigger for the developing of the HTx program. Our results suggest that the LVADs, mainly HeartMate 3, can be an alternative treatment of patients with end-stage heart failure in a country with a restricted HTx program.
Sensitivity of the S/D velocity ratio at the LVAD inflow cannula as an index for the detection of LVAD pump thrombus
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Purpose: LVAD pump thrombus (PT) is a serious complication that occurs in 8% of LVAD recipients and often requires LVAD pump exchange surgery. Formation of a thrombus inside of a left ventricular assist device (LVAD) constitutes an obstruction to forward flow, which worsens with time and eventually produces pump failure. When clots form in the LVAD, they often grow slowly over time, eventually occluding the LVAD inflow, a progression that is difficult to detect with current treatment standards. Oftentimes, thrombosed LVAD patients will present with high hemolysis and LDH, but these are nonspecific markers. Most patients with thrombus will have difficulty with LVAD unloading, indicating a clot has formed. However, by that point, the thrombus is usually too large to treat with increased anticoagulant therapy and a pump exchange must be performed. Pump replacement can be avoided if thrombus formation is detected early and treated with a careful titration of anticoagulants. The goal of the proposed research is to develop a method for early thrombus detection in LVAD patients by characterizing how the LV flow patterns in the LVAD-assisted heart change with simulated pump thrombus in a mock circulatory loop. Recently, the S/D velocity ratio of the LVAD inflow cannula has been identified as a sensitive index. Our goal in this study was to assess the S/D velocity ratio and other flow-based indices in the detection of PT using a mock circulatory loop.

Materials and Methods: Experimental studies were performed with a silicone model of the LV with dilated cardiomyopathy and the HeartMate II LVAD (St. Jude/Abbott). Neutrally buoyant fluorescent particles were added to a viscosity-matched blood analog solution. A LaVision PIV system captured a 40 Hz ensemble-averaged image sequence of the 2-D velocity field of the LV midplane for the cardiac cycle. A range of LVAD speeds were tested from 8-11krpm at baseline (BL) and during PT, which was simulated with a small disk centered over the rotor inflow housing that reduced the orifice area by 60%. Aortic pressure, aortic flow and LVAD flow were measured continuously at 200 Hz. Vortex structures were computed from the 2-D velocity field data by calculating the vorticity and using the Q criterion to identify the vortex boundaries. Vortex circulation, kinetic energy (KE), size, shape and position were calculated during the cardiac cycle. Localized velocity was evaluated in small regions of interest (ROI) in and around the inflow cannula, and maximum systolic (S) and minimum diastolic (D) velocities calculated.

Results and Discussion: A 7% decrease in LVAD flow and an increase in the proportion of outflow through the aortic valve were observed with PT. The ROI analysis of the LVAD inflow cannula revealed that D increased with LVAD speed, but decreased with PT. S/D for PT (10.0) was 80% higher than for BL (5.6) at 8krpm, 60% higher at 9.6krpm (BL=4.9, PT=7.8), and 40% at 11krpm (BL=4.2, PT=5.9). A comparison of the results to clinical data showed that the model produced S, D and S/D values within the clinical range.

Conclusion: Overall, PT increased resistance to LVAD inflow that increases with LVAD speed. Although the PT had a small effect on hemodynamics, the S/D ratio reflected a nearly two-fold increase over the range of LVAD speeds when compared to the BL values. Additional pump thrombus obstruction levels will be tested to determine the detection limit.

Body Composition Measurement Methods In Systolic Heart Failure Patients Receiving Left Ventricular Assist Devices
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Amanda R Vest, William W Wong, Corinne Pellows, Nathan Yuen, Angelo DeNofrio, Seth N Meltzer, Michael S Kiernan, David DeNofrio, Greg Couper, Edward Saltzman

Background: Sarcopenia is the age-related loss in fat-free mass (FFM) and deterioration in skeletal muscle function. FFM measurement is challenging in heart failure (HF) patients where a left ventricular assist device (LVAD) may affect dual energy X-ray absorptiometry (DXA) FFM values. In addition, increased extracellular water (ECW) volume can inflate FFM measurements by either the DXA or deuterium (DEU) dilution methods. We aimed to determine agreement between FFM measured by DXA vs DEU methods in advanced HF. We also assessed whether FFM changes at 3 months post-LVAD
implantation.

Methods: We conducted a pilot study with visit 1 at &lt;30d pre-LVAD and visit 2 at 90d (±14d) post-LVAD implantation.

FFM was measured each visit by both DXA (Hologic, Bedford, MA; Discovery A; v12.6.2:3; calculated total FFM and appendicular FFM/height2) and an oral 0.1g/kg deuterium oxide (DEU) + 1g sodium bromide (BRO) dilution study with blood sampling at 4 hours (using standard equations for total body water, TBW, and ECW, respectively). The agreement between FFM-DXA and FFM-DEU was assessed using Bland-Altman plots, with bias and precision statistics. We used Wilcoxon paired sign-rank tests to compare pre/post FFM values, and Spearman coefficients for the correlation between percent changes in FFM-DXA and FFM-DEU.

Results: Eight male advanced systolic HF patients were recruited, with mean age 61y and BMI 27kg/m2. All completed visit 1 (mean 9d pre-LVAD) and 7 completed visit 2 (mean 98d post-LVAD). Per standard DXA criteria, 5 subjects were sarcopenic pre-LVAD. Agreement between FFM measurements by DXA and DEU was high, with bias -3.0 (SD 5.0) and 95% limits of agreement -12.7 to 6.8. Mean values pre- v post-LVAD were: FFM-DXA 59.3 v 57.7kg (p=0.94); appendicular FFM/height2 7.9 v 7.6kg/m2 (p=0.47); FFM-DEU 56.6 v 54.5kg (p=0.47). The correlation in pre-post percent change was high between FFM-DXA and FFM-DEU: r=0.89 (p=0.012). The ECW:TBW was in the normal range both pre- and post-LVAD (0.34, 0.39) and so FFM values did not require adjustment for elevated ECW.

Conclusions: There was strong agreement between DXA and DEU measurement of FFM, even without using appendicular DXA values to avoid thoracic LVAD artifact. This suggests that either FFM method can be used for sarcopenia assessment in advanced systolic HF. There was no FFM change at 3 months post-LVAD amongst 7 systolic HF patients.

Changes In Glycemic Control And Body Mass Index In Left Ventricular Assist Device Patients With Diabetes

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Amanda R Vest, Cindy Chen, Jenica N Upshaw, Michael S Kiernan, Gregory S Couper, David DeNofrio

Introduction: Patients with type 2 diabetes mellitus (DM) and systolic heart failure (HF) often show improved glycemic control and reduced diabetes medication requirements after left ventricular assist device (LVAD) implantation. However, LVAD recipients also show increased body mass index (BMI) over time. We sought to determine whether post-LVAD improvements in hemoglobin A1c (HbA1c) are affected by changes in BMI.

Methods: We recruited 20 subjects with advanced HF and DM (HbA1c 6.5% or DM medications) and recorded HbA1c, BMI and DM medications pre-LVAD and at 1, 3 and 6 months of LVAD support. We constructed mixed effects linear regression models to separately examine the change in HbA1c and BMI over the same period and adjusted for markers of hemolysis and inflammation.

Results: Mean age was 61y, with 80% male and 75% ischemic HF. Pre-LVAD, 75% required DM therapy (60% scheduled insulin: mean 24h dose 58±61 units), vs 65% at 3 months post-LVAD (41% insulin: 45±36 units, p=0.035 vs pre-LVAD).

Pre-LVAD HbA1c was 6.9 ±0.9%. The decrease in HbA1c post-LVAD attenuated over time: at 1 month, 5.5% (p value for 1 month v pre-LVAD, p&lt;0.001, n=17); at 3 months, 6.3% (p=0.047, n=16); at 6 months, 6.5% (p=0.575, n=12), Fig 1. Pre-LVAD BMI was 27.3 ±3kg/m2 and trended upwards to 29.2kg/m2 by 6 months (p=0.143, n=12), Fig 1. The change in HbA1c and BMI over 6 months from pre-LVAD were significantly associated (t=3.76, p=0.001), even after adjustment for change in hemoglobin (hemolysis) and neutrophil-lymphocyte ratio (inflammation), (t=3.67, p=0.002).

Conclusions: In this small cohort of HF patients with DM, medication requirement and HbA1c significantly decreased early during LVAD support. Improvements in HbA1c were not sustained to 6 months, a finding that was statistically associated with an increase in BMI. Weight gain during LVAD support may attenuate the improvements in glycemia seen after stabilization of advanced HF.
**Chronotropic Incompetence and Rate Responsive Pacing in Patients with LVAD**

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Miguel Alvarez Villela, Thiru Chinnadurai, Kalil Salkey, Snehal Patel, Ulrich Jorde

**Purpose** Chronotropic incompetence (CI) is common in advanced heart failure and is associated with worsened functional capacity (FC). In patients with LVAD who have restored resting cardiac output, the consequences of CI on functional capacity, as well as the role of rate-responsive pacing (RRP) remain unclear.

**Methods** Patients with CF-LVAD in our heart failure clinic were tested with cycle or treadmill based CPX and 6MWT. Continuous ECG monitoring was provided during CPX. CI was defined as a peak HR of <80% of age predicted maximal HR (age-220). In a subgroup of patients, CPX and 6MWT were repeated after activation of RRP. Timing and pattern of RRP was determined from the ECG tracings during CPX.

**Results** Thirty patients were included, age was 49±15y, 30% were women and 70% had NICMP. Time on LVAD support was 20±17 months. LVADs were HeartWare in 3 subjects and HeartMate II in 27 patients. Nineteen patients had ICD (5 dual-chamber and 12 single-chamber) and 7 CRT. Baseline CPX’s were done on treadmill for 20 patients and cycle ergometer for 10, with a peak RER of 1.2 ± 0.1. The prevalence of CI (peak HR <80% APMHR) was 70%.

Patients with CI were more likely to have a pVO2<14ml.kg.min-1 (p=0.01) and had a lower peak HR (116±21 vs. 143±16; p=0.003) and peak oxygen consumption (pVO2) value (11.5±3 vs.14±2 ml.kg.min-1; p=0.02). Submaximal HR (HR@VT: 100 ±17 vs. 118 ±20; p=0.03) and oxygen consumption (VO2@VT: 8.7±2.7 vs. 10.3 ±2.5; p=0.10) were also lower. 6MWT distance was lower in patients with CI (290±91 vs. 340±64 m; p=0.3). A majority of patients were on beta-blocker therapy (93%). A significant correlation was present between heart rate response (ΔHR) to VT and VO2@VT (r=0.5, r²=0.24, p=0.005), as well as between ΔHR to peak exercise and pVO2 (r=0.6, r²=0.36, p<0.001), indicating that heart rate response is a strong determinant of exercise performance. Thirteen patients underwent repeat testing after RRP activation. All CPXs in this group were treadmill based. Pacing settings were VVI-R in 6 patients and to DDD-R in 7 depending on device type. Ten had Medtronic devices, 2 Boston Scientific and 1 St Jude Medical. After RRP activation, 6MWT distance increased significantly at a whole cohort level; 307±84 to 353 ±86m; p=0.001. During CPX, RRP did not commence in 7 patients and was inadequate in 2, starting early and stopping before reaching VT in one patient, and starting after VT was crossed in another patient. Neither of these patients saw an increase in VO2@VT while pVO2 increased by 7% and 4% from baseline respectively.

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Making the Case for Complex Bi-Ventricular Shock: From Profiling to Uncoupling to Recovery
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Jose A. Rodriguez-Arciniega MD, Mara Slawsky MD PhD, Gregory Valania MD, Amir Lotfi MD, Evan Lau MD, Jaime A. Hernandez-Montfort MD MPH

57-year-old lady who presented as a transfer from outside hospital with working diagnosis of community-acquired pneumonia and pulmonary embolism based on subsegmental filling defects and consolidation on CTA with evidence of RV/LV/PA dilatation. The patient was recently diagnosed with esophageal cancer s/p chemorradiation treated with trastuzumab and a remote history of PE on warfarin.

Underwent rapid escalation of care within 12 hrs of admission due to worsening hypoxemia and hypotension associated with biological markers suggestive of myocardial, renal and hepatic injury in addition to rising lactate leading to intubation and mechanical ventilation and addition of 2 vasoactive agents (norepinephrine/dopamine). Bedside ECHO showed severe biventricular dysfunction and surrogates of elevated right atrial pressure, pulmonary artery systolic pressure right and left atrial pressures in addition to low estimated stroke volume index which was confirmed by right heart catheterization: RA 22 mmHg, PA 86/41 (54) mmHg and PCWP 30 mmHg with estimated CI 1.4 L/min/m2 and Ao 73/53 (63). There was no evidence of obstructive coronary artery disease with adequate size proximal femoral vasculature on angiography in addition to a substantial burden of paroxysmal atrial and ventricular arrhythmias.

Based on clinical, hemodynamic and imaging profiling and with the aid of simulation PV-Loop program patient was classified as experiencing severe biventricular cardiogenic shock with out of proportion PH due to LH disease in a hemometabolic stage and decision was made to proceed with concomitant left femoral temporary microaxial flow pump (Impella CP) with inhaled nitric oxide and high dose intravenous diuretics.

Patient came off vasoactives with marked improvement in hemodynamic profile and normalization of biological markers within the first 12 hrs and was transitioned from iNO to intravenous nitroprussiate extubated after 4 days with daily echocardiographic weaning trial focused on loading conditions and LVOT VTI. On day 7 at P2 decision was made to remove support with RA 5 mmHg PA 53/13 (26) mmHg and PCWP 12 mmHg with CCI 3.5 L/min/m2 and LVOT VTI 15 cm with qualitative normal RH function and interval improvement in LVEF from 10 to 25% prompting transition to oral neurohormonal blockade and further outpatient plans for CTEPH evaluation.

This case summarizes the value of hemodynamic situational awareness in complex cardiogenic shock in which RV-PA uncoupling associated with possible CTEPH and chemotherapy induced acute myocardial injury required integration of therapies such as selective pulmonary vasodilators and high-profile percutaneous temporary mechanical circulatory support.

Smyd1a overexpression suppresses functional decline in the adult myocardium
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Marta W. Szulik, Li Wang, June Garcia-Llana, Christopher Tracy, Sarah Franklin

Heart disease is the leading cause of death in the United States. This chronic condition affects the heart so it can no longer sufficiently pump blood to vital organs in the body. While heart disease can manifest in many different ways the general pathophysiology is conserved: the heart compensates for an increased workload by undergoing hypertrophic growth, accompanied by transcriptional reprogramming, and progresses into heart failure. Although many epigenetic factors have been identified which influence these underlying changes in transcription during disease, we still know very little about how this process is regulated in the cardiomyocyte. Smyd1, a unique histone methyltransferase that regulates gene expression in the cardiomyocyte, was originally shown to play a crucial role in early cardiac development. More recently we have shown that loss of Smyd1 in the adult mouse heart leads to pro-hypertrophic signaling resulting in cardiomyocyte growth, fibrosis and functional decline. In addition, we examined the two Smyd1 isoforms (Smyd1a and Smy1b) in isolated myocytes and showed that Smyd1a (but not Smyd1b) overexpression (OE) was capable of inhibiting phenylephrine-induced hypertrophy. To further characterize the role of Smyd1 in the myocardium and determine if Smyd1a is capable of inhibiting hypertrophic growth in adult mice we generated transgenic mice capable of
inducible, cardiac-specific OE of Smyd1a using a Tet-On system. Mice were fed doxycycline laced chow for 2 weeks to achieve Smyd1a-OE at which time we characterized their cardiac phenotype under basal conditions and after stress (permanent occlusion). Interestingly, transgenic mice showed no observable difference under basal conditions, however, 3 weeks after permanent occlusion of the LAD, the EF of wild type animals decreased to ~37%, while transgenic mice maintained an EF of ~61%. In addition, transgenic mice exhibited exacerbated growth (12% increase in HW/BW ratio) with no change in expression of the hypertrophic marker ANF, in contrast to wild type animals (4-fold increase). These exciting results suggest that Smyd1a is capable of preserving cardiac function in adult mice, however, this mechanism appears to be independent of hypertrophic signaling.

Cardiogenic Shock and Short-Term Mechanical Circulatory Support Options in the Current Era: Focus on Adverse Events

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Background: In the absence of robust evidence from randomized controlled trials, clinicians treating cardiogenic shock (CS) often make decisions on short-term Mechanical Circulatory Support (s-t MCS) based on individual center or clinical team preferences. We sought to investigate whether description of device-related adverse events (AE) could help identify targets to advance the field.

Methods: Our institution’s CS database was queried for CS patients who underwent placement of s-t MCS based on predefined criteria, between Jan 2014 – Mar 2017. After excluding post-cardiotomy CS and those who required central cannulation, we identified 79 who required s-t MCS with Intra-Aortic Balloon Pump (IABP), Impella, peripheral Veno-Arterial Extra-Corporeal Membrane Oxygenation (VA-ECMO) or combination of these options.

Results: 18 patients (22.7%) were treated with IABP, 23 (29.1%) with Impella, 10 (12.6%) with VA-ECMO and the remaining 28 (35.4%) with combinations of devices. Severity of CS at presentation revealed no significant differences in blood pressure, heart rate, number of Inotropes/pressors, left ventricular ejection fraction, use of mechanical ventilation and CPR. The VA-ECMO compared with IABP, Impella and Combination groups had higher lactate (11.0 vs 7.2 vs 5.1 vs 5.3, p=0.007) and lower pH (7.0 vs 7.1 vs 7.2 vs 7.2, p=0.004) pre-MCS. The mean length of support was similar between IABP, Impella, VA-ECMO groups and was longer in the Combination Vs Impella group (p=0.005). Major AE are shown in the Table. The mean ICU stay was 14 days and did not differ among the groups. Exchange to durable LVAD was performed in 7 patients: 1/18 (IABP), 3/23 (Impella) and 3/28 (Combination) group. The overall survival to hospital discharge was 45.5% and did not differ between the groups (p=0.2).

Conclusions: Despite significant advances in the technology of s-t MCS options, morbidity and mortality remain high and the device-related AE could provide practical quality improvement targets for CS programs.

Decreases in Sympathetic Innervation Following Transition to Sacubitril/Valsartan in the REMODEL (Reverse Remodeling Effects of Entresto) Study

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Gabriel Sayer, Sara Kalantari, Sarah Tayazime, Gene H Kim, Nitasha Sarswat, Jayant Raikhelkar, Parker Ward, Roberto Lang, Nir Uriel

Background: Sacubitril/Valsartan is an angiotensin receptor - neprilysin inhibitor that was shown to significantly reduce the rate of death and heart failure hospitalization in patients with heart failure and reduced ejection fraction. The mechanism underlying the benefits seen with sacubitril/valsartan over standard medical therapy for heart failure is unknown. The REMODEL study investigated the effect of sacubitril/valsartan on ventricular remodeling, including sympathetic nervous system activity as measured by 123-meta-iodobenzylguanidine (MIBG) scintigraphy.

Methods: In this prospective, single-arm longitudinal study, 40 patients on stable HF therapy were initiated on sacubitril/valsartan after a two week run-in period of ACE or ARB alone. MIBG scintigraphy was performed prior to initiation of sacubitril/valsartan and after 3 months of treatment. Echocardiography, exercise capacity and quality of life measures were obtained at the same time points. MIBG results were compared using paired t-tests.

Results: 40 patients were enrolled. The mean age was 56 ± 12 years, 25 (63%) were male and 11 (28%) had an ischemic
cardiomyopathy. The majority of patients were New York Heart Association Class II. At baseline, the late heart-to-mediastinal (H/M) ratio was 1.37 ± 0.20 and the washout rate was 47.3%. After three months of therapy with sacubitril/valsartan, the late H/M ratio increased by 0.12 ± 0.11 (p<0.001), and the washout rate decreased by 11 ± 16% (p<0.001; Figure 1A and 1B).

Conclusions: Addition of sacubitril/valsartan to baseline heart failure therapy resulted in a decrease in cardiac sympathetic activity, as shown by a decrease in the late H/M ratio and an increase in the washout rate on MIBG imaging. The decrease in sympathetic nervous system activity can explain the improvement in survival seen with sacubitril/valsartan and may serve as a good measure of medication response.

**Functional Assessment of decellularized extracellular matrix in patients undergoing LVAD implantation**
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Purpose: Changes within the extracellular matrix (ECM) are a critical myocardial adaptation that occurs during cardiac remodeling and can be the result of changes in composition, structure, and function. We aim to determine the changes in functional properties of ECM obtained from myocardial tissue samples at the time of LVAD implant and at the time of transplant. We hypothesize that assessment of these ECM properties may lead to the identification of myocardial conditions more suitable for recovery or conditions suggesting an irreversibly diseased state.

Methods: Myocardial tissue samples were obtained at the time of LVAD implantation. Samples underwent decellularization followed by histologic analysis and scanning electron micrography (Figure 1A). The material properties of the decellularized ECM were measured using compression testing and rheology. We measured the storage modulus (G'), as an assessment of elastic properties, loss modulus (G''), as an assessment of viscous properties, and Young’s modulus (slope of stress-strain curve) as a measure of material stiffness.

Results: Ten myocardial samples have been obtained and analyzed at the time of LVAD implant. Mean age is 53.4 years (range 31-70). Eight subjects are male (80%) with ischemic etiology in 3 (30%). Mean ejection fraction (EF%) was 19.1% ± 8.8%. Storage modulus of the ECM between patients can be plotted to assess for differences between subjects (Figure 1B). Subjects with pulmonary capillary wedge pressure < 25mmHg demonstrated a trend toward higher Young’s modulus (8845 ± 2569 Pa vs 3056 ± 594.3 Pa, p=0.15) Figure 1 C.

Conclusion: The functional properties of decellularized ECM obtained at the time of LVAD implant can be assessed and may demonstrate an independent parameter for ECM function. Comparison to the paired samples at the time of transplantation will be important to understand the ECM contribution to reverse remodeling and myocardial recovery.

**REMODEL: Reverse Remodeling Effects of Entresto (valsartan/sacubitril)**
Nir Uriel, MD, University of Chicago, Chicago, IL

Authors: Sara Kalantari, Diego Medvedofsky, Jonathan Grinstein, Sarah Tayazine, Gene H. Kim, Nitasha Sarswat, Sirtaz Adatya, Jayant Raikelkhar, David Beiser, Parker Ward, Roberto Lang, Gabriel Sayer, Nir Uriel.

Background: Valsartan/sacubitril, an angiotensin receptor-neprilysin inhibitor, significantly reduced the rates of death from any cause and from cardiovascular causes as well as the rates of hospitalizations for worsening heart failure as compared to a target-dose enalapril-based regimen for patients with HFrEF. The pathophysiology underlying the benefit of valsartan/sacubitril and its effects on remodeling remain unknown. Here we seek to further elucidate the benefits of valsartan/sacubitril on ventricular remodeling and functional status.

Methods: In this prospective, single-arm longitudinal study, 40 patients were initiated on valsartan/sacubitril after a two week run in period of ACE or ARB alone. The primary end-point was the degree of reverse remodeling (change in LV and RV size, volume, shape, and function) as assessed by 3D-TTE with surface analysis at 3 months compared to baseline using paired t-tests. Secondary endpoints were peak VO2 and 6-minute walk distance.
Results: Interim analysis of 24 patients shows significant reduction in LV and RV volumes with improvement in LV conicity and sphericity indices at 3 months (Table 1). Interim analysis revealed improved 6-minute walk distance (440 ± 97 vs 466 ± 98 m; p = 0.007) and no change in peak VO2 (18.5 ± 5.4 vs 18.8 ± 4.7; p = 0.56) at 3 months.

Conclusion: This is the first study to investigate the effects valsartan/sacubitril on ventricular remodeling and functional status at 3 months. Interim analysis suggests improved remodeling.

LVAD versus BiVAD-mediated allosensitization in bridge-to-transplant patients
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Background: Ventricular assist devices (VADs) have been associated with the development of anti-HLA antibodies due perhaps to immune-activating properties of the VAD itself. We aimed to characterize differences in HLA antibody formation in adult patients receiving left- (LVAD) versus biventricular- (BiVAD) assist devices as bridges to transplantation (BTT).

Methods: Assessment for anti-HLA antibodies was performed before, and at multiple time-points following VAD implantation. Serum alloantibodies were detected with a cytotoxic panel-reactive antibody (PRA) method until 2003, an ELISA method from 2003 to 2005 and SAB assays on the Luminex platform from 2005 to 2017. Sensitization was defined either as PRA >10%, or as peak anti-HLA antibody mean fluorescence intensity (MFI) values of more than 1000. Baseline characteristics and sensitization in the two patient groups were evaluated using descriptive statistics.

Results: Between 2003 and 2017, 134 patients were placed on VAD support at our institution as BTT. Sensitization data were available for 130 patients. Forty two (32.3%) patients were supported with an LVAD (median age, 48 years, 26.2% female) and 88 (67.7%) with a BiVAD (median age, 45 years, 28.4% female). Twenty-three (54.8%) of the LVAD and 47 (53.4%) of the BiVAD patients were eventually transplanted (p=0.9) with an average time to transplantation 588 and 562 days respectively. Eleven (26.2%) LVAD and 33 (37.5%) BiVAD patients died before transplantation (p=0.4) with an average time on VAD support before death 269 and 302 days respectively. Evidence of sensitization pre-VAD was found in 17.1% of the LVAD and 12.5% of the BiVAD patients (p=0.9); these percentages rose to 40.0% (p=0.03) and 43.7% (p=0.001) respectively at 2 to 7 months post-VAD implantation. However, the post-VAD sensitization status was not statistically different between the LVAD and the BiVAD group (p=0.7). Among the 23 LVAD patients who were transplanted 7 (30.4%) were sensitized immediately pre-TX, compared to 22 (46.8%) out of 47 BiVAD patients (p=0.2).

Conclusion: VADs are a factor of de novo anti-HLA antibody development in adult patients after implantation. The resulting sensitization pattern is not significantly different between LVAD and BiVAD patients in the early post – implantation period.