**032**

**Minute Ventilation-Targeted Adaptive Servo Ventilation Improves Subendocardial Injury in Acute Decompensated Heart Failure Patients as Assessed Through Decreases in High-Sensitivity Cardiac Troponin I**

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**Introduction:** Minute ventilation targeted adaptive servo ventilation (MV-ASV) therapy has been shown to decrease pulmonary edema and mitigate sleep disordered breathing (SDB) in patients with acute decompensated heart failure (ADHF). Cardiac Troponins represent subendocardial ischemia and necrosis in these patients, and elevations are associated with poor outcomes. Troponin elevation might be mitigated by treatment with MV-ASV therapy.

**Hypothesis:** MV-ASV therapy should mitigate troponin elevation in patients admitted with ADHF compared to those under standard therapy.

**Methods:** This is a pilot study in which twenty-one consecutive patients with ADHF were randomized to either MV-ASV therapy (S9 VPAP Adapt, ResMed Corp.) with standard care, or standard care alone. MV-ASV therapy was administered for a minimum of six hours per day for up to 5 days, or until discharge. Daily High-Sensitivity Troponin I (hsTnI) levels were measured with SMC™ technology (Singulex). Results: hsTnI was detected in all patients (mean 53.9pg/mL for the MV-ASV group and 12.5pg/mL for the standard group). Most patients on MV-ASV had some drop in hsTnI levels during hospitalization. By the end of day three, the mean hsTnI decreased by 23.1pg/mL (42.9%) in the MV-ASV group but only decreased by 1.3pg/mL (10.4%) in the standard group. Patients with the highest levels of hsTnI at admission appeared to have the most benefit by MV-ASV.

**Conclusions:** The use of MV-ASV in patients with ADHF resulted in a greater decrease in hsTnI levels, signaling a treatment-induced reduction in subendocardial injury.

**Figure 1.**

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**033**

**Relationship Between Serum Neuregulin Level and Subsequent Cardiac Function Among Patients with Systolic Heart Failure**

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**Background:** Neuregulin-1/β (NRG), via ErbB2/ErbB4 receptor stimulation, is an epidermal growth factor that participates in cardiomyocyte function, growth, survival, repair, and response to stress. NRG has been shown to improve left ventricular (LV) function in animal models after ischemic injury. However, little is known about the intrinsic physiologic response of NRG in human systolic heart failure (HF).

**Methods:** Serum NRG levels were measured using enzyme linked immunosorbant assay among patients with systolic HF, defined as LV ejection fraction (LVEF) <55%, on optimal medical management. Serial measurements of LVEF were recorded over the course of 1 year. Clinical characteristics were compared to assess the physiological relationship between baseline NRG levels and change in LVEF (categorized as no change, ≥10% decrease or ≥10% increase).

**Results:** Of 198 patients (baseline LVEF of 25±10), 106 had non-ischemic HF (mean age 55±13 years, 65% males) and 92 had ischemic HF (mean age 62±12 years, 87% males). Cohort consisted of 60% hypertensives, 38% diabetics, 65% with dyslipidemia and 51% with history of smoking. Mean New York Heart Association (NYHA) class was 2.7 (±0.7). We found that 98 patients had no change in LVEF, 76 had increase and 24 had decrease in LVEF. Those with ≥10% drop in LVEF were more likely to have worse NYHA class (2.7 ±0.7) and ischemic HF (58%) compared to those with ≥10% increase in LVEF (2.5 ±0.7 for NYHA class and 33% with ischemic HF; p<0.05 for both). Patients with decrease in LVEF had lower NRG levels (mean 6.5 ng/ml) compared to those with no change or increase in LVEF (mean 20 ng/ml). Also patients with worse NYHA class tended to have higher NRG levels; NYHA class I (mean 6.0 ng/ml) and NYHA class IV (mean 19.7 ng/ml).

**Conclusion:** Serum NRG levels appear to be higher among patients with worse NYHA class and those with no change or ≥10% increase in LVEF over the course of the study. These results suggest that NRG may play a reparative or protective role in cardiac adaptation to pathological stimuli and may have prognostic or therapeutic value. Further studies are needed to better define its function.

**Figure 1.**

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**034**

**The Clinical Implications of Cardiac Troponin I Measured by an "Ultrasensitive" Assay in Acute Decompensated Heart Failure: Insights from ASCEND-HF**

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**Introduction:** Circulating cardiac troponins (cTn) are commonly elevated in patients with heart failure. Highly sensitive cTn assays detect circulating cTn at 1/10th and lower compared to standard cTn assays. Very low levels of cTn detected by these assays may be prognostically informative and they may be used as a continuous variable for prognostic assessment. Hypothesis: Circulating cTn measured by a novel, ultrasensitive assay during acute heart failure (AHF) are associated with short- and long-term clinical outcomes.

**Methods:** cTnI was measured in a core-lab by an ultrasensitive immunoassay (SMC technology, Singulex, LOD 0.78 pg/mL) in 900 consecutive patients with AHF enrolled in the ASCEND-HF (n-esirintide vs. placebo) biomarker substudy. Patients were excluded with clinical evidence of an acute coronary syndrome or cTn >5x the URL. Multivariable adjustment, with variables derived from the main ASCEND-HF population, were used to determine the per-unit-change association between cTnI and short- to long-term outcomes. cTnI was natural log-transformed.

**Results:** All patients (age 66±15 y, 32% female, EF 32±15%, 73% NYHA III-IV, and NT-proBNP 5791 [2986-11579] pg/mL) had cTnI levels above the LOD at baseline. 5791 (83%) had cTnI levels above the 99% URL (7.1 pg/mL). Of these 751, 90% remained above the URL by 48-72 hours and 82% by 30-days. Higher baseline cTnI was associated with a higher risk of death or worsening heart failure prior to discharge (OR 1.38, p=0.02) and death at 30 days (OR 1.26, P=0.01), or death/heart failure rehospitalization at 30 days (OR 1.10, P=0.4). The ultra-sensitive cTnI had a higher NRI for death at 180-days (19.6%) than the standard sensitivity (TnI assay 1%), in addition to the ASCEND clinical models when both were measured (N=798). Conclusions: CtnI remained elevated on follow-up testing in the majority of patients with cTnI greater than the 99% URL at baseline. Higher cTnI was independently and incrementally
associated with a higher risk of death and worsening heart failure prior to discharge and 180-day mortality.

**035**

**Association Between Serum Ghrelin Levels and Congestive Heart Failure: A Meta Analysis**

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**Background**: Ghrelin is a gut derived peptide hormone and an endogenous ligand of growth hormone secretagogue receptor implicated to play a role in cardiovascular physiology. Cardioprotective effects of ghrelin were demonstrated on experimental heart failure models however the mechanism remains unclear. It is hypothesized that ghrelin mediates cardiac autonomic nervous system activity and prevents angiotensin 2 mediated apoptosis of cardiomyocytes. We conducted a meta-analysis to evaluate the relationship between serum ghrelin levels and Congestive heart failure (CHF).

**Methods**: We searched MEDLINE, CINHAL and COCHRANE databases for studies reporting serum ghrelin levels in the CHF and non CHF study population. We included case controls, cohort and cross-sectional studies. We calculated the weighted standardized mean difference (SMD) in serum ghrelin levels between the CHF and control groups.

**Results**: Our search strategy yielded 118 articles and we included 9 studies enrolling 674 participants. The median age of the CHF group was 67 yrs. (IQR 61-70) compared to 64 yrs. (IQR 57-67) in the control group. The median body mass index in the CHF group was 25 kg/m² (IQR 24-28) compared to 23 kg/m² (IQR 23-28) in the control group. The median body mass index in the CHF group was 25 kg/m² (IQR 24-28) compared to 23 kg/m² (IQR 23-28) in the control group. The median percentage of female population in the CHF group was 31% (IQR 19-39) compared to 39% (IQR 29-49) in the control group. The unweighted median serum ghrelin levels in the CHF group were 223 pg/ml (IQR 62.2 - 640) compared to 177 pg/ml (IQR 70-669) in the control group. The SMD of serum ghrelin level was -0.346 (95% CI -0.513, -0.179) p = 0.001 comparing CHF to non CHF study population.

**Conclusion**: Serum ghrelin levels are significantly and inversely associated with CHF. Further studies are needed to investigate the role of ghrelin in the development of CHF and evaluate its efficacy as a novel biomarker and its therapeutic potential in patients with CHF.

**Figure 1.**

**036**

**Adrenomedullin Helps Risk Stratify Patients With Pre-Clinical Diastolic Dysfunction**

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**Background**: The significance of pre-clinical diastolic dysfunction is unclear. Strategies to further risk stratify this subset of patients may help determine who will progress and require closer follow up. Adrenomedullin gene expression has been shown to correlate with cardiovascular events (CVE) such as stroke, acute coronary syndrome, and cardiac related death (CRD). Bioactive Adrenomedullin (bio-ADM) is a novel biomarker for serum level of adrenomedullin that has not yet been studied for clinical utility in pre-clinical diastolic dysfunction.

**Methods**: We conducted a single center prospective cohort study of 200 Veterans undergoing outpatient echocardiography over a 4 year period. Only patients with Stage B diastolic dysfunction were included in the analysis. All patients with systolic dysfunction and clinical evidence of heart failure were excluded. EDTA-blood samples were obtained to analyze levels of bio-ADM (Sphingotec GmbH, Hemnspgdorf, Germany) at the time of echocardiography. We used multi-variable Cox-regression analysis to generate hazard ratio (HR) and 95% confidence intervals (CI) for categorical stratification of bio-ADM value. Follow up time was at one-year from enrollment in the study.

**Results**: Of the 200 consecutive patients enrolled, 44 had evidence of pre-clinical diastolic dysfunction and made up the study cohort. The study cohort was 98% male and had an average age of 66.9 ± 1.4. There were 14 events in this cohort corresponding to a one year CVE rate of 31.8%. Receiver Operator Curve analysis identified 31.15 pg/mL, as having maximal sensitivity and specificity. Chi squared analysis showed patients above this cut-off had an elevated odds ratio for CVE at one year (4.173; 95% CI 1.27-5.33). Kaplan-Meier curve for event free survival demonstrated significantly worse prognosis for patients with ADM values above 31.16 pg/mL (4.5; p = 0.034). Patients below ADM cut-off showed enhanced prognosis at one year follow up (HR 0.134; [95% CI 0.027-0.662]).

**Conclusions**: In patients with pre-clinical diastolic dysfunction, bio-ADM may help identify those at highest risk for cardiac events.

**Figure 1.**

**037**

**Renal Biomarkers Predict Adverse Outcomes in Heart Failure with Preserved Ejection Fraction**

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**Background**: Heart failure with preserved ejection fraction (HFpEF) accounts for approximately 25-50% of all heart failure diagnoses. HFpEF has a heterogeneous population and exerts significant mortality and morbidity, yet remains challenging to prognosticate. To identify prognostic factors in HFpEF, we sought to test the relevance of biomarkers and transthoracic echocardiogram (TTE) parameters as predictors of heart failure (HF) hospitalization in HFpEF patients.

**Methods**: This was an observational prospective study of patients admitted to our cardiology service in 2013 for HFpEF. Diagnosis of HFpEF was made using Framingham clinical criteria for HF, a serum NT-proBNP above the ICON study group’s rule-in cut-off point and a contemporaneous TTE ejection fraction (EF) ≥ 50%. We also evaluated the time to mitral annulus early diastolic velocity (E’E) for all patients. One-year follow-up data on admissions for heart failure and length of stay was obtained from hospital records. Correlation analysis was done using Spearman’s rank-order correlation.

**Results**: We identified 48 patients with HFpEF. Our HFpEF population was 47.9% female, with a mean age of 71.9 ± 13.5 years. Mean serum urea, creatinine, and estimated glomerular