

**P-057****Gene Expression of Inflammatory Marker in Myocardial Biopsy May Predict Progressive Heart Disease**

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**Background:** Some studies suggested that analysis of gene expression in myocardial biopsy promised to improve the differential diagnosis of heart failure. On the other hand, higher serum inflammatory markers are known to predict worse prognosis in heart failure without infectious complication. **Objective:** We examined whether gene expression of inflammatory markers in myocardial biopsy predicted one subgroup of patients with progressive heart disease, indicative of ongoing immune activation. **Method:** We examined gene expression of inflammatory markers/leukocyte markers, inflammatory cytokine and chemokine by quantitative RT-PCR in heart samples from patients admitted to our hospital due to heart failure/ cardiac biopsy, 55; autopsies, 5. **Result:** Gene expression of several inflammatory markers was detectable from a small piece of cardiac biopsy. Expression levels of inflammatory markers in samples of myocarditis were higher than those of non-myocarditis. But expression levels of inflammatory markers in some samples of non-myocarditis, progressive heart diseases like Fabry disease and mitochondrial cardiomyopathy, were the same as those of myocarditis. **Conclusion:** High expression of leukocyte marker, inflammatory cytokines and chemokine may predict progressive heart disease, albeit infiltrating immunocompetent cells are not detected histopathologically.

**P-058****Decreased Serum BDNF Levels are Correlated with Lower Exercise Capacity in Patients with Heart Failure**TAKA AKI FURIHATA<sup>1</sup>, SHINTARO KINUGAWA<sup>1</sup>, ARATA FUKUSHIMA<sup>1</sup>, TSUNEAKI HOMMA<sup>1</sup>, YOSHIHIRO MASAKI<sup>1</sup>, TAKAHIRO ABE<sup>2</sup>, SHINGO TAKADA<sup>1</sup>, TOMOYASU KADOGUCHI<sup>1</sup>, KOICHI OKITA<sup>3</sup>, HIROYUKI TSUTSUI<sup>1</sup><sup>1</sup>Department of Cardiovascular Medicine, Hokkaido University Graduate School of Medicine, <sup>2</sup>Department of Rehabilitation Medicine, Hokkaido University Graduate School of Medicine, <sup>3</sup>Graduate School of Lifelong Sport, Hokusho University

**Background:** Depression is highly prevalent in patients with heart failure (HF) and one of independent predictors for its adverse outcomes. Brain derived-neurotrophic factor (BDNF) is involved in the pathogenesis of cardiovascular disease and skeletal muscle metabolism as well as depression. We thus investigated whether serum BDNF was associated with depressive symptoms, cardiac dysfunction, and exercise capacity in HF patients. **Methods and Results:** Forty three consecutive patients with HF (57.4±14.8 years old, New York Heart Association class I-III) and 27 age-matched healthy subjects as controls (52.2±8.8 years old) were studied. HF patients had significantly lower serum BDNF levels than controls (17.5±4.9 vs. 24.6±5.8 ng/mL, P<0.001). HF patients had lower peak VO<sub>2</sub> and anaerobic threshold (AT) and higher depressive symptoms according to the BDI and PHQ-9 scores. By univariate analysis, peak VO<sub>2</sub> (r=0.372, P=0.016), AT (r=0.324, P=0.043), and triglyceride (TG) (r=0.455, P=0.002) were significantly correlated with serum BDNF levels among HF patients. There was no significant association between depressive symptoms or cardiac dysfunction and serum BDNF level. By multivariate analysis, peak VO<sub>2</sub> was identified as an independent determinant of serum BDNF levels (β-coefficient=5.03, 95% CI [1.64, 8.42], P=0.004). **Conclusion:** Decreased serum BDNF levels were significantly associated with exercise capacity in HF patients, suggesting that they can be a useful biomarker for predicting exercise intolerance associated with HF.

**P-059****Clinical Features between Mild and Severe Central Sleep Apnea in Chronic Heart Failure**YOKO YAMADA, HIROSHI WADA, KENICHI SAKAKURA, NAHOKO IKEDA, YOSHITAKA SUGAWARA, JUNYA AKO, SHIN-ICHI MOMOMURA  
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**Introduction:** Central sleep apnea (CSA) is commonly observed in patients with heart failure (HF). The aim of this study was to elucidate the clinical significance between mild CSA and severe CSA patients with HF patients. **Methods:** We enrolled 1120 patients who were admitted to our institute with the diagnosis of HF between 2006 and 2012. Among them, 334 underwent screening of type III sleep monitor and 280 patients were diagnosed with SDB. SDB was defined as > 5/hour of apnea-hypopnea index (AHI). The details of SDB, 218 (78%) were OSA and 62 (22%) were CSA. Among CSA, 43 showed severe CSA (AHI > 30/hour). **Results:** In severe CSA, male sex, higher BMI, larger LVDD and Ds, larger LAD, and lower LVEF was significant compared to mild CSA. There was no significance in medication. **Conclusions:** The clinical features between mild CSA and severe CSA with HF were different. As beta-blockers are known to reduce the severity of CSA in patients

with HF, more aggressive treatment might be required to severe CSA. This study suggested that CSA was one of an important target to treat HF.

**P-060****Efficacy and Safety of Indacaterol and Glycopyrronium Bromide in Patients with COPD and Heart Failure**SHIRO NAKAMORI<sup>1</sup>, KATSUYA ONISHI<sup>1</sup>, NAOKI ISAKA<sup>2</sup>, YUJI UEDA<sup>5</sup>, HIDEKI TANAKA<sup>4</sup>, MITSUHIRO YOSHIDA<sup>6</sup>, SHINYA OKAMOTO<sup>3</sup>, MASA AKI ITO<sup>1</sup><sup>1</sup>Department of Cardiology, Mie University Graduate School of Medicine, <sup>2</sup>Department of Internal Medicine, Murase Hospital, <sup>3</sup>Department of Internal Medicine, Iwasaki Hospital, <sup>4</sup>Department of Internal Medicine, Tanaka Internal Clinic, <sup>5</sup>Department of Internal Medicine, Ueda Clinic, <sup>6</sup>Department of Internal Medicine, Yoshida Clinic

**Backgrounds and purposes:** COPD is a frequent co-morbidity in heart failure (HF), and co-existing COPD further worsens prognosis in HF patients. However, COPD has been undertreated because bronchodilators may increase heart rate (HR) in HF patients. Accordingly, the purpose of this study is to examine whether inhaled long acting beta2 stimulator (indacaterol) and long acting anti-cholinergic inhibitor (glycopyrronium bromide) does not affect HR in patients with COPD and HF. **Methods & Results:** We recruited 50 patients with COPD and stable HF (age: 74±8 y.o.). Office blood pressure (BP) and pulse rate (PR), and mean BP and PR at home were measured, and spirometry, ECG, and laboratory examination including BNP were performed before and 3 months after treatment with indacaterol (n=40) or glycopyrronium bromide (n=10). The forced expiratory volume in one second (FEV1) was significantly improved (1.18±0.54 vs. 1.34±0.63 L). Office and home BP were unchanged, but office and home PR and HR in ECG were significantly decreased. Plasma BNP levels were significantly decreased after treatment. **Conclusion:** Conventional treatments of COPD with indacaterol or glycopyrronium bromide decreased HR and BNP in COPD patients accompanied with HF. Thus, patients with HF and COPD could safely tolerate indacaterol or glycopyrronium bromide, which may have favorable effects on HF.

**P-061****The Direct Effect of Adaptive Servo-ventilation on the Hemodynamic Fluctuation in Patients with Heart Failure and Sleep-disordered Breathing**NAOTO KUMAGAI<sup>1</sup>, KAORU DOHI<sup>1</sup>, TADAFUMI SUGIMOTO<sup>2</sup>, YUICHI SATO<sup>1</sup>, KIYOTAKA WATANABE<sup>1</sup>, MUNEYOSHI TANIMURA<sup>1</sup>, HIROSHI NAKAJIMA<sup>1</sup>, NORIKAZU YAMADA<sup>1</sup>, MASHIO NAKAMURA<sup>3</sup>, MASA AKI ITO<sup>1</sup><sup>1</sup>Department of Cardiology and Nephrology, Mie University Graduate School of Medicine, <sup>2</sup>Department of Cardiology, Ise Red Cross Hospital, <sup>3</sup>Department of Clinical Cardiovascular Research, Mie University Graduate School of Medicine

**Background:** The direct effect of adaptive servo-ventilation (ASV) on hemodynamics in patients with heart failure (HF) concomitant with sleep-disordered breathing has not been fully investigated. **Methods:** We enrolled 14 patients with HF (64±13 years old, NYHA 2.2±0.7, LVEF 37±12%). All patients underwent repeated overnight polysomnography (Embla N7000) and simultaneously continuous beat-by-beat hemodynamic measurements (Task Force Monitor, Nihon-Kohden) including heart rate, mean blood pressure (MBP), stroke volume index, and total peripheral resistance index (TPRI) at baseline and during ASV (Auto-Set CS, Teijin Co.), respectively. The hemodynamic fluctuations associated with periodic nocturnal apnea-hypopneas were assessed quantitatively by spectral analysis using maximum entropy method (MemCalc system). The ratio of spectral power in 0.01-0.03 Hz, which coincides with frequency of apnea-hypopneas, to the total power in the total frequency band (0.003-0.5 Hz) was used as index of hemodynamic parameter variability, named normalized spectral power (NSP) at 0.01-0.03Hz. **Results:** Apnea hypopnea index during ASV was significantly lower compared to baseline (18.0±13.2 vs. 43.5±24.8/hour). Whereas ASV did not change average hemodynamic parameters, NSP at 0.01-0.03Hz in MBP and TPRI were significantly reduced by ASV (0.25±0.09 vs. 0.36±0.15, and 0.18±0.09 vs. 0.23±0.11, p<0.05, respectively). **Conclusion:** ASV therapy stabilized periodic fluctuations of MBP and TPRI in patients with HF.

**P-062****Correlation between Plasma Midkine Levels and Sleep Disordered Breathing in Patients with Chronic Heart Failure**

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**Background:** Midkine is a 13-kDa growth factor whose expression has shown to be up-regulated under hypoxic stress. We have reported that elevated serum midkine is an independent predictor of cardiac events in patients with chronic heart failure