(8-OHdG), a marker of oxidative stress, was related to LV remodeling in dilated cardiomyopathy (DCM). **Methods:** We performed full study of cardiac catheterization including endomyocardial biopsy from LV in 35 patients with DCM (left ventricular ejection fraction (LVEF)=28±5%). Biopsy samples were stained with sirius red to evaluate myocardial fibrosis, and also stained with immunohistochemical method using anti-8-OHdG antibody to evaluate myocardial oxidative stress. In 150 DCM patients, moreover, we examined whether urinary 8-OHdG levels correlated with LVEF, LV end-diastolic volume index (LVEDVI) and LV mass index (LVMI), peak early diastolic mitral annulus velocity (e')by echocardiography. **Results:** Biopsy samples data showed that the ratio of oxidized nuclei in cardiomyocytes and CVF were significantly increased in patients with DCM as compared with normal subjects. A direct correlation was found between the positive staining ratio of nuclei and CVF (n=35, r=0.64, P<0.001). Urinary 8-OHdG was also significantly higher in DCM patients than in control subjects (DCM; n=150: 13.5 ±3.1 ng/ml vs control; n=30: 8.0±1.9 ng/ml, P<0.001). There was a significant correlation between urinary 8-OHdG and LVEF, or LVEDVI, e'. **Conclusions:** These findings suggest that urinary 8-OHdG may be a clinically-useful marker for LV remodeling associated with DCM.

O-010

Urinary 8-hydroxy-2′-deoxyguanosine as a Novel Marker for Predicting the Inflammatory Activity in Patients with Cardiac Sarcoidosis

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Here, we investigated whether urinary (U) 8-hydroxy-2′-deoxyguanosine (8-OHdG), a marker of oxidative stress, predicts inflammatory activity in cardiac sarcoidosis (SAR). **Methods and Results:** Immunohistochemical examination in the autopsy samples of left ventricle (LV) obtained from a SAR patient, revealed positive staining for 8-OHdG on the LV sections corresponding to the focus with accumulation of ^{18}F-FDG by PET/CT. Serum 8-OHdG was significantly higher in coronary sinus than in aorta in active SAR patients. Moreover, we measured U-8-OHdG in 30 control subjects, 25 DCM patients and 32 SAR patients. All patients with SAR underwent ^{18}F-FDG PET/CT to evaluate the inflammation status for dividing active SAR (n=20) and non-active SAR (n=12). U-8-OHdG in SAR was higher than that of control subjects. U-8-OHdG in active SAR was higher than that of non-active SAR or DCM. In ROC curve analysis, U-8OHdG powerfully predicted active SAR (AUC: 0.97; 95% CI 0.91-1.02) from all SAR patients. The optimal cutoff value for prediction of active SAR was 14.8 ng/mg creatinine. In a multivariate regression analysis, U-8-OHdG was an independent predictor of active SAR (HR5.5; 95% CI 0.798-3.118, p<0.019). U-8-OHdG levels in active SAR patients were significantly decreased after corticosteroid treatment, in proportion with a decrease in the focal pathological tracer uptake in heart. **Conclusion:** These findings suggest that U-8-OHdG presents a novel and powerful predictor of active SAR.

O-011

Acute Hypertensive Heart Failure Patients Show Paradoxical Hemoconcentration on Admission

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Background: Though decongestion/diuretic therapy are started immediately after admission in acute heart failure syndrome (AHFS), changes in hemoglobin in this period remain to be investigated. **Method and Results:** Changes in hemoglobin between on admission and 24±12 hours postadmission were evaluated in 143 AHFS patients. Patients with cardiogenic shock, hemodialysis, blood transfusion, and/or urgent coronary angiography were excluded. In spite of immediate decongestion/diuretic therapy (urine output of 1600±990mL/ 24h postadmission), hemoglobin on admission was paradoxically **higher** than the level of 24h postadmission in 104 patients (73%). Admission hemoconcentration, defined as the top tertile of baseline-to-24h **decrease** of hemoglobin (δHb), was more prevalent (43%) in hypertensive AHFS (systolic blood pressure (SBP); >140 mmHg) than normotensive/hypotensive AHFS (15%, p<0.001). δHb correlated with initial SBP (r=0.50, p<0.001) and heart rate (r=0.30, p<0.001), suggesting sympathetic effect on hemoconcentration. Patients with hemoconcentration had lower ejection fraction (30±11 vs. 39±15% p=0.002), higher presence of severe congestion on chest radiography (85% vs 60%, p<0.01), night time admission (60% vs. 27%, p<0.001), and dependence on mechanical ventilation (35% vs. 7%, p<0.001) than those without hemoconcentration. Urine output in 24h, age, sex, creatinine, and presence of ischemic origin are comparable between two groups. **Conclusion:** Hypertensive AHFS shows paradoxical hemoconcentrateion on admission, which may associate with sympathetically mediated fluid shifts from circulating volume to extracellular spaces and reflect severe congestion.

O-012

Serum BNP Level is the Predictor of Long Prognosis of Flash Pulmonary Edema

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Background: Flash pulmonary edema (FPE) is a clinical term used to describe a particularly dramatic form of acute decompensated heart failure (ADHF). However, clinical profile of FPE is still remained unclear, especially the predictor of long prognosis is little known. **Methods:** We investigated database (nCASCADE) for ADHF, to assess the patients with FPE who was defined as acute respiratory distress caused by pulmonary edema that required treatment with mechanical ventilation (with NPPV or tracheal intubation) and began within 6 hours of seeking medical attention. nCASCADE database is a uni-center registry designed to prospectively collect data on each episode of hospitalization for ADHF, since July 2006 every patient whose diagnosis at discharge as ADHF were enrolled. In this study, 757patients were analyzed who enrolled from July 2006 to June 2010. **Results:** The patients with FPE (58 patients; 7.6%) showed significant difference of hypertension, coronary artery disease, atrial fibrillation, systolic BP and respiratory rate, and more severe pulmonary edema but not volume overload. Kaplan Meier analysis revealed no significant difference of the long-term prognosis in both groups. IN univariate analysis, serum BNP level at discharge was the only predictor of long prognosis. **Conclusion:** Serum BNP level at discharge was the only predictor of long prognosis in the patients with FPE.

O-013

Post-Traumatic Stress Disorder after the Fukushima Daiichi Nuclear Plant Disaster in Patients with Cardiovascular Diseases -The CHART-2 Study-

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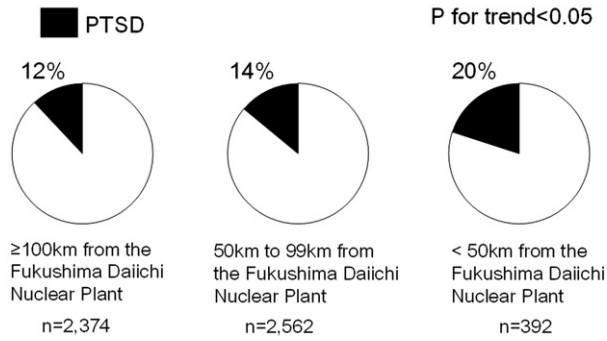
Background: The aim of this study was to investigate psychological stress from the Fukushima Daiichi Nuclear Plant Disaster in patients with cardiovascular diseases (CVD). **Methods:** Post-traumatic stress disorder (PTSD) was defined when the event scale-revised (IES-R) exceeded 24 points. According to the distance from the plant, the prevalence and clinical characteristics were studied in 5,328 CVD patients (mean age, 68±11 years; male, 70%) from the Chronic Heart Failure Analysis and Registry in the Tohoku District-2 (CHART-2) study. **Results:** The prevalence of PTSD was negatively correlated with the distance from the nuclear plant (Figure). The patients with PTSD were characterized by higher prevalence of female genders, non-smokers, and NYHA III-IV functional class. **Conclusion:** The Fukushima Daiichi Nuclear Plant Disaster caused psychological damage to the patients with CVD.

Figure. The prevalence of PTSD after the Fukushima Daiichi Nuclear Plant Disaster (N=5,328)



O-014

Distinct Prognostic Factors in Patients with Chronic Heart Failure and Atrial Fibrillation

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Purpose: To compare prognostic factors between CHF patients with and without atrial fibrillation (AF). **Methods:** We examined consecutive 527 CHF patients (479 males, age 59±14 years) who underwent cardiopulmonary exercising testing (CPX),

echocardiography and blood examination at the same time before discharge in our hospital. Patients were divided into two groups: AF group (n=130) and non-AF group (n=397). We compared blood testing data, exercise capacity, cardiac function and prognosis between CHF patients with AF and non-AF groups. Patients were followed up (average period: 381±239 days) to register cardiac deaths and re-hospitalization due to worsening heart failure. **Results:** There were 89 cardiac events during follow up period. Cardiac event rate was significantly higher in AF group than in non-AF group (26.2% vs 13.9%, P<0.001). In non-AF group, multivariate Cox hazard analysis demonstrated that body mass index (Hazard ratio (HR): 0.703, P<0.01), log BNP (HR: 3.039, P<0.01), deceleration time (HR: 0.987, P<0.05), peak VO_2 (HR: 0.784, P<0.05) and exercional periodic breathing (HR: 3.689, P<0.01) were independent factors to predict adverse clinical outcomes. On the other hand, sodium concentration (HR: 0.864, P<0.01), hemoglobin concentration (HR: 0.746, P<0.05) were independent parameters to predict cardiac events in AF group. **Conclusions:** Prognostic factors were different between CHF patients with and without AF, and this should be considered to manage CHF patients with AF.

O-015

Gender Differences in the Clinical Features of Hypertrophic Cardiomyopathy Caused by Cardiac Myosin-binding Protein C Gene Mutations

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Objectives: Although gender may be one of the important modifying factors in hypertrophic cardiomyopathy (HCM), there has been little information on it. **Methods:** We investigated gender differences in the clinical features of HCM caused by cardiac myosin-binding protein C gene (*MYBPC3*) mutations. Sixty-one subjects (28 families) with MYBPC3 mutations were studied. **Results:** Of 61 subjects with the mutations, fifty patients were phenotype-positive by echocardiography. The disease penetrance in subjects aged < 40 was 92.3 % in males and 66.7 % in females. In those patients with phenotype-positive, females were diagnosed with HCM at 50 ± 19 years old, while males at 45 ± 14 years old. Female patients were more symptomatic at diagnosis than males (Mean New York Heart Association class was 1.70 ± 0.77 versus 1.22 ± 0.42, p=0.012). From longitudinal point of view, no significant differences were identified between the genders with genotype-positive in terms of cardiovascular deaths and cardiovascular events. During the follow-up period from their diagnosis of HCM (11 ± 8 years), female patients with phenotype-positive had significantly more frequent heart failure events than did phenotypically affected male patients (p=0.028). **Conclusions:** Although females with *MYBPC3* mutations showed later onset of the disease, female patients were more symptomatic at diagnosis and had more frequent heart failure events when once they developed hypertrophy.

O-016

Impact of Short-duration Adaptive Servo-ventilation Therapy on Cardiac Function in Patients with Heart Failure

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We investigated whether short-duration adaptive servo-ventilation (ASV) therapy improves cardiac function in heart failure (HF) patients. Eighty-six consecutive HF patients were divided into three groups: group A patients underwent daily ASV therapy for a mean duration of > 4 h; group B patients used ASV therapy for > 1 to < 4 h per day; and group C patients declined or could not have daily ASV therapy for > 1 h. The frequency in ASV use did not significantly differ between groups A (79.3±19.2%) and B (70.9±17.4%). After 6 months, a significant increase in left ventricular ejection fraction (LVEF), significant decrease in plasma BNP levels and decrease in LV end-diastolic volume (LVEDV) were observed in groups A ([LVEF] 5.0±8.1%, [BNP] -24.9±33.7%, [LVEDV] -6.2±10.1%) and B ([LVEF] 3.5±5.5%, [BNP] -16.5±24.6%, [LVEDV] -5.1±8.2%) as compared with group C ([LVEF] -1.5±6.0%; p=0.004, p=0.017, [BNP] 2.8±10.2%; p=0.002, p=0.017, [LVEDV] 0.8±9.1%; p=0.031, p=0.043). Significant correlation was shown between the total ASV use time and changes of LVEF (r=0.369, p=0.002), BNP (r=0.445, p< 0.001), and LVEDV (r=-0.374, p=0.001). Admission rate was lower in group A (4.1%) and B (7.1%) than in group C (25%, log-rank test; p=0.042, p=0.045). Multivariate analyses showed that the frequency in ASV use was a strong parameter for the improvement of LVEF (coefficient=0.284, SE=0.035, p=0.019). ASV therapy improves cardiac function in HF patients even with short-duration usage.

O-017

Urinary Concentration of Neutrophil Gelatinase-associated Lipocalin and Risk of Acute Kidney Injury in Patients Hospitalized for Worsening Heart Failure

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We prospectively investigated the predictive value of admission urinary levels of neutrophil gelatinase-associated lipocalin (NGAL), a new marker of acute kidney disease (AKI), for the development of AKI in 167 consecutive patients hospitalized for worsening heart failure. AKI was defined as a greater than 50% increase in creatinine (Cr) from the baseline or absolute increase of <0.3 mg/dl within 48 hours after admission. **Results:** Patients with AKI (n=20) had a higher tendency inhospital mortality rate than those without (25% vs 13%, P=0.1), Clinical characteristics according to quartiles of urinary NGAL were shown in Table. In a stepwise logistic analysis, urinary NGAL (P=0.0004), but not urinary albumin excretion, was independently associated with AKI. **Conclusion:** Higher admission urinary level may be a powerful and independent risk factor of AKI in this population.

Table

Quartiles of uninary NGAL (ug/gCr)	1st < 16.5 n=42	2nd 16.5-44.4 n=42	3rd 44.4-159.5 n=43	4th > 159.5 n=41	P value
Age (years)	73.5	75.5	78.0	76.0	0.2
Diabetes(%)	52.4	33.3	34.9	41.5	0.4
Previous history of old Myocardial infarction(%)	57.1	42.9	44.2	48.8	0.5
Estimated GFR (ml/min/1.73m)	56.7	52.6	49.2	33.3	0.003
BNP(pg/ml)	618.5	589.5	732.0	1000	0.046
Alb(g/dl)	40.9	688	141.0	885.8	0.0001
Sex(male %)	71.4	64.3	55.8	31.7	0.0001

O-018

Inhibition of Adipose Inflammation as a Novel Therapeutic Target for Heart Failure

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Accumulating evidence has indicated the close link between insulin resistance and heart failure (HF). Recent studies have also shown that adipose inflammation plays a crucial role in the development of insulin resistance. Here we show that p53-induced adipose tissue inflammation is critically involved in insulin resistance during HF and that inhibition of adipose inflammation improves the progression of cardiac dysfunction as well as metabolic abnormalities. We found that insulin resistance developed in two murine models of HF. HF markedly up-regulated p53 expression in adipose tissue in association with an increase of adipose tissue inflammation. Increased sympathetic activity promoted lipolysis that led to accumulation of oxidative stress and DNA damage. This accumulation resulted in the up-regulation of adipose p53 that induced adipose inflammation and insulin resistance via the NF-κB-dependent pathway. We found a detrimental vicious cycle in which HF induces insulin resistance that in turn accelerates cardiac dysfunction. Inhibition of lipolysis by sympathetic denervation significantly down-regulated adipose tissue p53 expression and inflammation, thereby improving insulin resistance but also cardiac dysfunction. Likewise, disruption of p53 activation in adipose tissue ameliorated inflammation in this tissue and improved insulin resistance, but also improved cardiac dysfunction associated with HF. Our results suggest that inhibition of p53-induced adipose tissue inflammation could be a novel therapeutic target to block the metabolic vicious cycle in patients with HF.

O-019

Inhibition of CaMKII/ERK-Mediated eNOS Phosphorylation Impairs Endothelial Function in Renal Failure Mice: New Effect of AsymmetricDimethylarginine

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Background: Patients with chronic kidney disease (CKD) showed the elevation of circulating asymmetric dimethylarginine (ADMA). Recent studies suggested that ADMA impairs endothelial nitric oxide synthase (eNOS) via effects other than competition with the substrate L-arginine. We sought to identify the molecular mechanism by which increased ADMA causes endothelial dysfunction in a CKD model. **Methods and Results:** In wild-type mice, 5/6 nephrectomy increased blood urea nitrogen and serum creatinine by 2.5- and 2-fold, respectively, and elevated circulating ADMA by 20% without blood pressure change. Nephrectomy deteriorated endothelium-dependent relaxation and reduced eNOS phosphorylation of isolated aortic rings. In transgenic (TG) mice overexpressing dimethylarginine dimethylaminohydrolase-1, the enzyme that metabolizes ADMA, circulating ADMA was decreased to half that of wild-type mice and