methyliodophenylpentadecanoic acid) in the hypertrophic myocardium was observed in 2 patients. Genetic analysis revealed the presence of α-GalA gene mutation in 2 cases. **Conclusions**: Heterzygous FD is not rare in symptomatic patients with female HCM. Endomyocardial biopsy is a helpful diagnostic tool for heterozygous FD. Distribution of hypertrophic portion and metabolic-perfusion mismatches vary from patients to patients in this disease.

PJ-445

Negative Inotropic Effect Induced by Cyclic GMP Would be an Underlying Mechanism of Takotsubo Cardiomyopathy

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Background; Underlying mechanism of takotsubo cardiomyopathy (TAKO) remains unclear. Methods; BNP, adrenaline (AD), noradrenalin (NA), dopamine (Dopa), cyclic AMP (cAMP), cyclic GMP (cGMP) and creatine kinase (CK) were measured in 10 subjects without organic heart disease, in 10 patients with acute myocardial infarction (AMI) and in 16 patients with TAKO. Blood samples were collected from the coronary sinus in each patient. Results; Although left ventricular dysfunction in TAKO was extremely severe as indicated by BNP, myocardial signaling pathway in response to catecholamines barely maintained as indicated by cAMP and cGMP. Part of the left ventricular dysfunction in TAKO would be caused by cGMP, which is known as negative inotrope. Conclusion; Negative inotropic effect induced by elevated cGMP in secondary response to excessive catecholamines would be an underlying mechanism of TAKO.

Comparison of sampling data in healthy subjects, AMI group and TAKO group

	Healthy subject	AMI	TAKO
BNP (pg/ml)	50.1 ± 13.9	97.0 ± 32.3	1086.0± 306.2*†
AD (pg/ml)	48.0 ± 7.1	28.7 ± 35.5	210.6 ± 70.1
NA (pg/ml)	250.4 ± 35.4	377.0 ± 73.5	1697.1 ± 323.1*†
Dopa (pg/ml)	9.6 ± 0.9	13.1 ± 3.0	78.4 ± 15.1*†
cAMP (pmol/ml)	8.8 ± 2.0	5.0 ± 2.0	16.1 ± 1.9*†
cGMP (pmol/ml)	3.3 ± 0.9	2.3 ± 1.0	11.3 ± 2.1*†
CK (IU/L)		1877 ± 571.6**	408.8 ± 183.0

*P <0.05 as compared to healthy subject. †P <0.05 as compared to AMI. **P <0.05 as compared to TAKO. Mean ± SD is shown.

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Effect of Autoantibodies Activating Human β1-Adrenergic Receptors on Cardiac Function and Clinical Outcome in Patients with Cardiac Sarcoidosis

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Background Although corticosteroids are generally indicated in patients with cardiac sarcoidosis (CS), a reliable marker for the monitoring of steroid treatment remains to be established in CS. Autoantibodies against the β1-adrenergic receptor (anti-β1-AR) are associated with severity of heart failure. We therefore hypothesized that the anti-β1-AR autoantibodies may be associated with clinical outcome in CS patients treated with steroids. **Methods** To test our hypothesis, we measured serum anti-β1-AR autoantibodies in 12 CS patients and 21 healthy controls using ELISA method. **Results** Anti-β1-AR autoantibody levels were higher in CS than the control group (10.4 ± 3.6U/ml versus 6.0 ± 3.0U/ml, $p<0.05$). CS patients before steroid treatment showed significantly higher autoantibody levels as compared to stable patients (11.6 ± 2.0U/ml versus 6.0 ± 0.6U/ml, $p<0.01$). The autoantibodies were higher in patients with LVEF<40% than those with LVEF≥40% (12.7 ± 1.1U/ml versus 8.0 ± 3.3U/ml, $p=0.053$). During a mean follow-up of 20 months, 3 patients had a cardiac event in spite of corticosteroid treatment. The autoantibody levels of the 3 increased 8.7 ± 0.8U/ml to 13.0 ± 1.4U/ml ($p=0.066$) during the follow-up period. The patients with a cardiac event showed significantly higher levels of anti-β1-AR autoantibodies as compared to event-free patients on corticosteroids (12.0 ± 2.0U/ml versus 6.0 ± 0.6U/ml, $p<0.01$). **Conclusions** Anti-β1-AR autoantibodies are associated with reduced cardiac function and clinical outcome in CS. This measurement may be helpful for the monitoring of CS patients treated with corticosteroids.

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Hepatocyte Growth Factor Gene Therapy in Doxorubicin-induced Cardiomyopathy

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Hepatocyte growth factor (HGF) has been reported to exert beneficial effects on myocardial infarction or hereditary cardiomyopathy. We here applied a gene therapy with HGF to murine model of doxorubicin (DOX)-induced cardiomyopathy. Two weeks later, adenovirus encoding human HGF gene was injected into the hindlimb muscles. Left ventricular dilatation and dysfunction persisted 2 more weeks later in controls, which were significantly mitigated in the HGF-treated mice. DOX-induced cardiomyocyte atrophy/degeneration and myocardial fibrosis were significantly attenuated by the HGF treatment. Among downstream signals of c-Met, extracellular signal-regulated kinase was inactivated by DOX, and the HGF treatment was found to restore its activity. This study presents novel signal pathways in efficacy of HGF on the heart with DOX-induced cardiomyopathy, and imply therapeutic efficacy of HGF gene therapy against established cardiac dysfunction.

PJ-448

3-Methylglutaconic Aciduria (3MGA) in Adult Patients with Left Ventricular Systolic Dysfunction (LVSD)

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Background: Barth syndrome is a rare disease caused by impaired leucine metabolism andcharacterised by 3MGA, dilated cardiomyopathy (DCM), neutropenia and skeltal myopathy. Majority of these patients died in infancy or early childhood, but several cases can survive until an adult period. This suggest the possibility that an abnormal amino acid metabolism might be responsible for DCM in adult. Therefore, we investigated the potential role of abnormal amino acid metabolism in patients with LVSD with unknown etiology. Methods: We measured 24 kinds of urinary amino acid and their metabolites in consecutive 23 patients (mean age 61 years old) with etiology-unknown LVSD by gas chromatography mass spectrometry. We also investigated 12 patients with hypertrophic cardiomyopathy (HCM) (mean 67 years old) or 14 controls (mean 56 years old) who showed normal ECG without any disease condition relating myocardial dysfunction. Results: An increased excretion (defined as greater than mean+SD of healthy controls) of 3-methylglutaconate was found in 3 patients (age 63,74,77 years old)with LVSD, but never found in HCM nor controls. In these 3MGA patients disease onset was 44, 55 and 70 years old and no one showed neutropenia and skeltal myopathy. Conclusion: These results suggest that 3MGA, an abnormal leucine metabolism, might be responsible for LVSD in adult.

PJ-449

Microcirculatory Dysfunction Accelerates Elevation of Plasma BNP Levels in Asymptomatic Non-obstructive Hypertrophic Cardiomyopathy

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[Purposes]: Coronary flow reserve (CFR) is known to be reduced in patients with hypertrophic cardiomyopathy (HCM). The plasma level of brain natriuretic peptide (BNP) is well correlated with the clinical severity of heart failure and hypertrophy. We investigated whether there is any prognostic linkage of BNP levels to CFR in patients with asymptomatic HCM. [Methods]: Twenty-eight asymptomatic patients with non-obstructive HCM were investigated. Doppler velocity catheters were introduced into the left anterior descending