Conclusion: NT-proBNP/BNP Ratio in concentration of pmol/L was significantly increased with the elevated concentration of BNP and/or NT-proBNP while that was not always coincident in NYHA-HF classification. When HF is getting worsened, NT-proBNP is getting relatively much higher than BNP in concentration. In short, concentration of NT-proBNP may reflect much more sensitively the severity of HF than that of BNP. NT-proBNP/BNP ratio will be a potent objective index to evaluate the severity of heart failure.

P4222 | SPOTLIGHT 2013
Relationship between serum fibroblast growth factor 23 levels and left ventricular mass measured by three-dimensional echocardiography in patients with end-stage renal disease

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Purpose: In patients with chronic renal insufficiency traditional risk factors of left ventricular (LV) hypertrophy include hypertension, overhydration, anemia and impaired calcium-phosphate homeostasis. Fibroblast growth factor 23 (FGF-23) is a phosphaturic hormone secreted by osteoblasts and a rising biomarker associated with LV hypertrophy and mortality in patients with end-stage renal disease (ESRD). We sought to determine the relationship between serum FGF-23 levels and left venticular mass measured by three-dimensional (3D) echocardiography in ESRD patients.
Methods: This retrospective cohort study included 44 patients (mean age 48±13 years, 54% men) with ESRD on three times per week maintenance hemodialysis. Exclusion criteria were previous history of diabetes and any significant cardiac disease. Beyond conventional transthoracic echocardiographic examination, 3D recordings were obtained using multi-beat reconstruction from 6 consecutive cardiac cycles (GE Vivid E9). After semi-automated tracing of LV endo- and epicardial surface at end-diastolic frame, LV mass was calculated using dedicated software (GE 4D Auto LVQ). Serum FGF-23 levels were measured by enzyme-linked immunosorbent assay (Merck Millipore). Overhydration was evaluated by bioimpedance (Fresenius Body Composition Monitor), laboratory test results (including serum calcium, phosphate, parathormone, total iron binding capacity levels) and blood pressure were recorded and averaged in the three previous months. Relationships were calculated by Spearman correlation test and multivariate linear regression.
Results: The median value of LV mass measured in ESRD patients was 244 grams (interquartile range 97.5). Serum FGF-23 levels ranged between 34 and 6848 with a median of 687 pg/ml. Serum levels of FGF-23 (ρ=0.52), phosphate (ρ=0.55), parathormone (ρ=0.38), total iron binding capacity (ρ=0.61), systolic blood pressure (ρ=0.38) and pulse pressure (ρ=0.47, all p<0.05) correlated significantly with LV mass. FGF-23 correlated with serum phosphate (ρ=0.83) and parathormone (ρ=0.53, both p<0.001) levels. In a multivariate linear regression model, FGF-23 (β=0.42, p<0.001), total iron binding capacity (β=0.49, p<0.001) and systolic blood pressure (β=0.37, p<0.01) were found to be independent predictors of LV mass.
Conclusions: To the best of our knowledge, this is the first study which demonstrates the strong correlation between serum FGF-23 levels and LV mass measured by 3D echocardiography. Beside the chronic volume- and pressure overload, LV hypertrophy is strongly determined by the endocrine effects of FGF-23 in patients with ESRD.

P4223 | BEDSIDE
Association between plasma indoxyl sulfate levels and cardiac hypertrophy in patients with heart failure

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Purpose: Although indoxyl sulfate (IS), one of a uremic toxin, is suggested be a novel prognostic marker in patients with chronic kidney disease, its clinical characteristics has remained uncertain in patients with heart failure (HF) and preserved renal function (RF). We aimed to determine the clinical characteristics of IS in patients with HF.
Methods: We studied 726 participants without overt HF and renal disease from a community-living, and prospectively enrolled 154 consecutive hospitalized acute and chronic heart failure (CHF) patients with preserved RF (eGFR >40 ml/min/1.73 m^2) (24 acute HF patients and 130 CHF patients, respectively). We also performed right heart catheterization (RHC) in CHF patients (n = 105).
Results: The plasma IS (PIS) levels in patients with CHF were significantly higher than that of healthy population matched with gender and eGFR of HF patients (0.79 [25th to 75th IQR: 0.45-1.19] μg/ml vs. 0.07 [0.04-0.11] μg/ml, respectively, p<0.001) (Figure A.), PIS levels were significantly correlated with right atrial pressure (r = 0.19, p = 0.028) and cardiac output (r = -0.30, p<0.001) in RHC study. Echocardiography revealed that LV mass index in High IS group (≥0.79 μg/ml) was significantly higher than that of Low IS group (<0.79 μg/ml) (Figure B.) in CHF patients. Interestingly, of 24 acute HF patients, PIS levels at discharge were

Figure 1
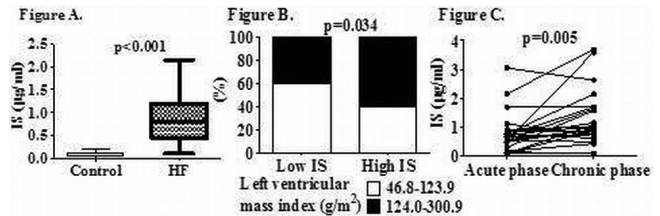
significantly elevated compared with the baseline, as preliminary data (0.67 [0.36-0.90] μg/ml to 0.94 [0.76-1.68] μg/ml, p = 0.005) (Figure C).
Conclusions: The plasma IS levels were suggested to be related to renal perfusion pressure with the prevalence of cardiac hypertrophy. From the change of IS levels during HF hospitalization, IS might be a novel marker to predict remote renal and cardiac status in patients with heart failure.

P4224 | BENCH
Can pulmonary sonography help in diagnosis of pulmonary congestion in sistolic and diastolic heart failure?

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Fluid retention and redistribution lead to pulmonary edema (PO), which is the cardinal manifestations of Heart Failure (HF). Diastolic Heart Failure (DHF) is the most common cause of increased pressure PO wich may be the only manifestation of DHF.
Material and methods: 380 patients with HF were evaluated. 86 patients DHF (I group) and 294 patients had systolic HF (II group). The control, III group consisted of 155 patients with left ventricular diastolic dysfunction but without HF. Sonographic examination of a lung was done with 3,0-4,0 MgHz convex or sector probe, from 10 points on thoracic wall (cross points of midclavicular line II, IV and V intercostal spaces and anterior axilar line with IV and V spaces), which corresponded to the projection of lower, middle and upper lobes of right lung and upper and lower lobes of left lung.
Results: During ultrasound examination 95,5% of patients with HF had "Comet tail phenomenon" (CTPh), which was registered only in 35,5% patients without HF (p>0,001). In DHF group CTPh was registered in 91,9% and in systolic HF group in 96,6% patients. In 81,4% of patients with DHF CTPh was registered from 3 and more registration points. In control group CTPh was registered from more than 3 points only in 2 (1,3%) patients. The best results in diagnosis of DHF can be achieved if we take "3 and more registration points" as a reference point for diagnosis of pulmonary congestion (sensitivity - 0,911, specificity - 0,942, positive predictive value 0,975).
Conclusion: In patients with HF during pulmonary ultrasound examination significantly often was registered CTPh. The count of registration points from the thoracic wall of CTPh 3 and > is sensitive and specific sign of HF.

P4225 | BEDSIDE
Insights into the epidemiology of incident Heart Failure (HF): outcomes of rapid HF access clinic applying the NICE guidelines

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Purpose: The onset of heart failure (HF) is associated with early increase in the risk of hospitalisation and mortality. The National Institute for Clinical Excellence (NICE) HF guidelines mandate prompt diagnosis and management of new cases of HF. Thus patients with suspected HF must have an echocardiogram and assessment by a clinical specialist within 2 weeks, if they had a previous myocardial infarction or if their serum natriuretic peptide (NTproBNP) is >2000 pg/ml; or within 6 weeks if their serum NTproBNP is 400-2000 pg/ml. We report the activity and the findings of the first 9 months after establishing a rapid access one-stop HF clinic implementing the 2010 NICE guidelines for suspected incident HF cases, serving an English city with a population of 550,000 people.
Methods: We established 3/week clinics with the capacity of 18 patients per week. We collected data on the patients attending the dedicated one-stop HF consultant-led clinic in the first 9 months to January 2013. The patients underwent electrocardiography and echocardiography on the same day of the clinic visit. We gathered data on NTproBNP, echocardiographic and clinical findings. We monitored the waiting time for the clinic to assess the adherence to the guidelines. Only incident cases of HF were accepted for review.
Results: In the first nine months of the service, we accepted 605 referrals, of whom 539 patients (90%) attended the clinic. Following formal assessment by a consultant cardiologist with interest in heart failure, electrocardiography and detailed echocardiography: 183 patients (34%) were found to have HF with left ventricular systolic dysfunction (HF-LVSD), 196 patients (36%) with HF and preserved left ventricular ejection fraction (HFPEF), 44 patients (8%) with HF due to valve disease and/or pulmonary hypertension and there were 116 patients (22%) with no evidence of HF. Therefore, NTproBNP > 400 pg/ml in patients with symp-

toms and signs of potential HF accurately predicted the diagnosis of HF in 78% of the patients. 90% of the patients referred to the clinic were seen within the time-frame stipulated by NICE guidelines. Assuming that all the patients with new symptoms and signs of potential HF are being referred to the service, this suggests the rate in our city of 564 new incident HF cases per annum (PA), which corresponds to a rate of 103 new cases/100,000 people PA.

Conclusions: The service proved the feasibility of implementing HF NICE guidelines in the real world. It gave us a real world insights into the incidence of HF in the community and a realistic picture of the incidence of HFPEF and HF-LVSD.

P4226 | BEDSIDE
Epicardial fat volume is inversely correlated with the degree of diastolic dysfunction and outcome in patients with heart failure with preserved ejection fraction

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Introduction: Epicardial adipose tissue has been linked to cardiovascular metabolism and inflammation and has been shown to predict prevalence and progression of coronary artery disease.

The aim of the present study was to assess epicardial fat volume in patients with heart failure with preserved ejection fraction (HFPEF) in terms of quantification and predictive value.

Methods: HFPEF was defined as serum NT-proBNP levels >220 pg/ml, E/e' by echocardiography ≥8, signs or symptoms of heart failure and preserved left ventricular ejection fraction (EF≥50%).

58 HFPEF patients and 34 controls were prospectively evaluated. All patients underwent right heart catheterization. CMR studies included the assessment of cardiac function and dimensions by standard cine sequences. Epicardial fat volume was quantified offline, using dedicated software.

Results: Epicardial fat volume ranged from 23 to 89ml (mean 49.3±16.2 ml; patients: 43.8±13.4 ml, controls: 58.6±16.6 ml; p<0.001). Epicardial fat volume was significantly correlated with E/e' (R=-0.37; p<0.001), NT-proBNP (R= -0.27; p=0.012), right ventricular size and function (R= -0.32; p=0.002 and R=0.40; p<0.001), left ventricular ejection fraction (R=0.36, p<0.001), left and right atrial size (R= -0.27, p=0.01; R= -0.34; p=0.001), mean pulmonary arterial pressure (R= -0.36, p=0.006), pulmonary capillary wedge pressure (R= -0.33; p=0.013), and pulmonary vascular resistance (R= -0.34; p=0.01). Epicardial fat volume was not correlated with gender, age, renal function, or body mass index.

All study participants were followed for 356±198 days. By Kaplan-Meier analysis, event-free survival was significantly worse in subjects with epicardial fat volume below the median of 43 ml (log rank p=0.038).

Conclusion: Epicardial fat volume is inversely correlated with diastolic dysfunction, serum NT-proBNP, invasive measures of pulmonary hypertension, but not total body fat. Decreasing epicardial fat volume predicts adverse outcome in HFPEF patients. The mechanism causing decreasing epicardial fat volume in advanced disease remains to be determined.

HEART FAILURE: MECHANISMS FOR PROGRESSION

P4228 | BEDSIDE
Clinical significance of tissue fibrosis and conduction abnormality in long-term prognosis in hypertrophic cardiomyopathy

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Purpose: This study evaluates the level of tissue fibrosis by RV biopsy in hypertrophic cardiomyopathy (HCM) patients and assessed its relevance to the long-term prognosis.

Methods: Of 494 consecutive HCM patients, 194 patients histologically diagnosed were enrolled (58±13 years old). The amount of fibrosis (%-area) in tissue samples from RV biopsy were quantified and classified into mild (<6%), moderate (6~17%) and severe (>17%). Hemodynamic, echocardiographic and electrophysiological parameters were also evaluated. Patients were followed and primary endpoint was adverse cardiac events; heart failure or lethal ventricular arrhythmias, and secondary endpoint was death from any cause.

Results: Degree of tissue fibrosis was associated with cellular diameter, LVEDP but not LVEF and BNP level. Patients with severe fibrosis had longer filtered QRS (fQRS), positive late potential by SAECG and positive fragmented QRS, resulting in a higher incidence of VT/VF. During 5±4 years follow-up, 92 (47%) patients had adverse cardiac events. The higher degree of fibrosis had a greater risk of following adverse events (Fig.1). Multivariate Cox analysis revealed that tissue fibrosis (>6%) and longer fQRS of SAECG had a greater risk of adverse cardiac events with hazard ratio: 2.01 (95% CI=1.02-4.20; p<0.05) and 1.11/10-ms (95% CI=1.03-1.19; p<0.01), respectively. Therefore, a scoring from severity of tissue fibrosis (0~2) and filtered QRS duration (0~2) was useful for risk stratification of adverse cardiac events in HCM (Fig.2). On the other hand, lower LVEF (p=0.008) and history of VT/VF (p=0.02) were the independent predictor for any cause of death.
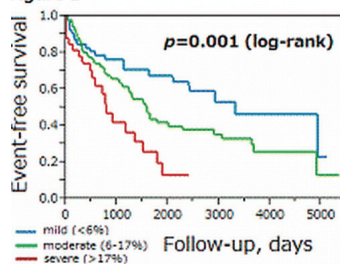
Cardiac events and tissue fibrosis
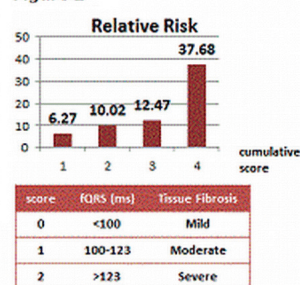
Conclusion: Higher LVEDP-related fibrotic change may contribute to the abnormal conduction delay as well as spontaneous VT/VF, leading to poor prognosis in HCM patients.

P4229 | BEDSIDE
Factors influencing transition to symptomatic heart failure in Stage-B asymptomatic patients -A report from the CHART-2 study

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Background: Increasing prevalence of heart failure (HF) is an urgent public health issue worldwide. Although the ACC/AHA Guidelines emphasize the importance to prevent the development of HF in asymptomatic Stage-B patients, little is known about the etiology and predictors for transition to symptomatic HF in Stage-B patients.

Method: Among the 10,219 subjects registered in our cohort, named as the Chronic Heart Failure Analysis and Registry in the Tohoku District 2 (CHART-2) study, we enrolled 4,463 Stage-B patients in the present study. We analyzed the predictors for de novo HF in asymptomatic Stage-B patients by Akaike's information criterion (AIC).

Results: Mean age was 67.3±12.4 years old, and male patients accounted for 71%. Regarding etiologies for asymptomatic cardiac structure abnormalities, the prevalence of ischemic heart disease, valvular heart disease, and cardiomyopathy was 51, 19, and 10%, respectively. During the median follow-up period of 3.0 years, 280 deaths (6.0%), 103 cardiovascular deaths (2.2%) and 165 de novo HF requiring hospitalization (3.5%) were noted. A stepwise Cox regression analysis with AIC revealed that development of de novo HF in Stage-B patients could be predicted by age (Hazard ratio (HR) 1.02, P=0.013), diastolic blood pressure (DBP) (HR 0.97, P=0.001), paroxysmal atrial fibrillation (PAF) (HR 2.50, P<0.001), chronic atrial fibrillation (CAF) (HR 2.20, P<0.001), left ventricular (LV) dilatation (HR 1.62, P=0.017), LV ejection fraction≤50% (HR 2.15, P<0.001), anemia (HR 2.02, P<0.001), chronic kidney disease (CKD) (HR 1.79, P=0.002), and statin use (HR 0.67, P=0.038). A sub-analysis showed that statin use was significantly associated with lower event rate of de novo HF in female patients (HR 0.41, P=0.009), older age (≥70 yrs.) (HR 0.56, P=0.011) and CKD (HR 0.60, P=0.041). Event rates of de novo HF in patients with PAF and CAF were comparable (2.2 vs. 2.3 events/100 person-years). In groups categorized by systolic blood pressure (SBP) and DBP, DBP lower than 70mmHg was a risk for de novo HF (HR 2.38, P<0.001), especially for patients with SBP ≥150mmHg (HR 9.39, P<0.001).

Conclusions: These results indicate that several factors could influence the progression from asymptomatic to symptomatic HF in Stage-B patients, including higher age (>70 yrs.), low DBP (<70mmHg), PAF, CAF, LV dysfunction (EF<50%), anemia, renal dysfunction and no statin use, suggesting that management of these factors could prevent the development of de novo HF in Stage-B patients.

P4230 | BEDSIDE
Soluble vascular endothelial growth factor receptor-2 serves as a predictor of cardiovascular events in patients with chronic heart failure

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Background: Vascular endothelial growth factor (VEGF) is a key regulator of cardiac angiogenesis and is required for preventing decompensated heart failure. Soluble VEGF receptor-2 (sVEGFR-2) acts as an endogenous inhibitor of VEGF. Recently, we demonstrated that serum sVEGFR-2 levels are increased in proportion to insulin resistance among subjects with metabolic syndrome. However, the significance of sVEGFR-2 levels in patients with chronic heart failure (CHF) is unknown.

Methods and results: We performed a prospective cohort study involving 117 symptomatic patients with CHF. Patients were followed up over 2 years. The pri-