Abstract P1523 – Table 1

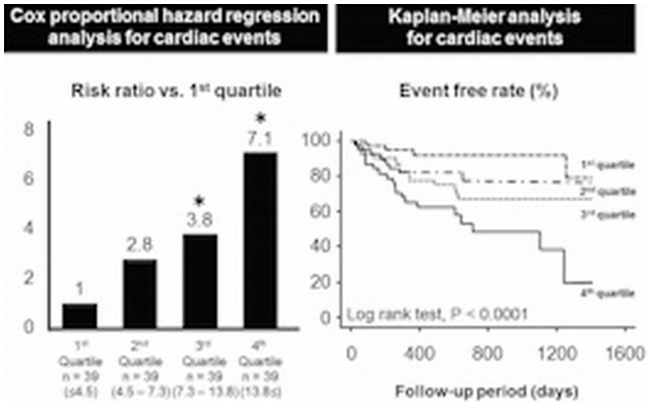
	LAV (ml/m^2)	LVDTE (msec)	LS (%)	GSRI (1/s)	UTRA (°/s)	TUTRA (msec)	RAV (ml/m^2)	PAPs (mmHg)	RVD (mm)	RVDTE (msec)	RVSRI (1/s)
HC	36±13	214±62	-19±8	0.94±0.2	-88±38	128±50	27±12	24±9	33±5	215±63	1.08±0.4
N	23±9	188±48	-22±4	1.19±0.2	-72±29	95±55	18±6	19±8	30±5	157±58	1.23±0.4
P value	<0.001	0.045	0.048	0.009	0.05	0.011	<0.001	0.005	0.023	<0.001	0.012

BNP, and delayed apical untwisting rate. All these findings correlated with the degree of liver dysfunction, suggesting an intrinsic cardiomyopathy generated by liver dysfunction.

P1524 | BEDSIDE
Plasma thioredoxin-1 level is associated with renal tubular damage and predicts poor prognosis in patients with chronic heart failure

Y. Otaki, T. Watanabe, H. Takahashi, H. Tamura, S. Nishiyama, T. Arimoto, T. Miyashita, T. Shishido, T. Miyamoto, I. Kubota. *Yamagata University, Yamagata, Japan*

Purpose: Oxidative stress plays a pivotal role in the progression of heart failure. Recent report showed that renal tubular damage (RTD), which is derived from renal parenchymal hypoxia, is a common risk factor for poor prognosis in patients with chronic heart failure (CHF). Thioredoxin-1 is an abundant 12.5 kDa redox-acting protein and is used as a reliable marker for oxidative stress. The aim of the present study was to determine whether plasma thioredoxin-1 level is associated with RTD and can predict cardiac prognosis in patients with CHF.
Methods and results: We measured plasma thioredoxin-1 level and urinary beta 2-microglobulin-creatinine ratio (UBCR) in consecutive 156 patients with CHF and 17 control subjects. Patients were prospectively followed during a median follow-up period of 627 days. There were 44 cardiac events. RTD was defined as a UBCR $\geq$ 300 μg/g, as previously reported. Plasma thioredoxin-1 was increased with advancing New York Heart Association (NYHA) functional class. Patients with RTD had higher thioredoxin-1 level than those without it. In the multivariate Cox proportional hazard analysis, elevated thioredoxin-1 level was independently associated with poor outcomes in patients with CHF after adjustment of confounding factors. A Kaplan-Meier analysis demonstrated that the highest 4th quartile of thioredoxin-1 level was associated with the highest risk of cardiac events.



Kaplan-Meiyer analysis

Conclusion: Plasma thioredoxin-1 level was associated with RTD and could risk stratify the patients at high risk in patients with CHF.

P1525 | SPOTLIGHT 2013
Reduced systemic arterial compliance and subclinical LV systolic dysfunction in COPD

J.M. Hilde[1], J. Hisdal[2], M.N. Melsom[1], V. Hansteen[2], I. Seljeflot[3], H. Arnesen[3], K. Steine[1]. *[1]Akershus University Hospital, Lorenskog, Norway; [2]Oslo University Hospital, Aker, Oslo, Norway; [3]Oslo University Hospital, Oslo, Norway*

Background: We hypothesized that COPD leads to alterations in systemic vascular structure and that systemic arterial compliance (SAC) would have impact on the LV function even in a population free of clinical cardiovascular disease.
Methods: Patients with COPD (GOLD stage I-IV) and matched healthy controls were included. Those with LV disease were excluded. Coronary heart disease was excluded by exercise ECG. The following TDI based indices for LV function were performed: LV acceleration during isovolumic contraction (LVIVA), myocardial performance-index (LVMPI) and peak systolic velocity (LVSm). SAC was calculated as stroke volume (ml)/systemic pulse pressure (mmHg). Inflammatory markers (Table) were measured.
Results: Consistent with reduced SAC, a significant increase in systolic blood pressure was observed in the patient group (Table). Stroke volume did not differ between the groups. Significantly higher levels of the biomarkers were found (all $p<0.01$) (Table). There were significant associations at $p<0.01$ between SAC and CRP and IL-6 in patients with COPD, but not in controls. Pulse pressure correlated with metalloproteinase (MMP-9), r=0.44 ($p<0.01$). LVEF was preserved; TDI measures for LV function were all significantly impaired in COPD (Table). SAC correlated significantly with LVIVA, LV Sm and LVMPI, r=-0.3, 0.4 and -0.3 ($p<0.01$), respectively.

Table 1

Variables (unit)	Controls (N=34)	COPD (N=100)
Systolic blood pressure (mmHg)	120±3	140±2*
Systemic pulse pressure (mmHg)	44±2.5	70±1.8*
Systemic arterial compliance (ml/mmHg)	1.8±0.7	1.1±0.7*
hsCRP (mg/l)	1.3±0.2	5.3±0.6*
Serum interleukin-6 (pg/ml)	2.1±0.3	4.4±0.3*
Serum matrix metalloproteinase-9 (ng/L)	228±19	598±33*
LVIVA (m/s^2)	1.7±0.1	1.3±0.1*
LVMPI (no unit)	0.36±0.01	0.56±0.01*
LVSm (cm/s)	9.9±0.2	7.7±0.1*

Conclusions: COPD patients showed subclinical LV dysfunction by TDI along with systemic inflammation, increased elastolytic activity and reduced arterial compliance, compared to controls. The reduction in SAC provides one mechanism for the observed LV dysfunction in these patients.

P1526 | BEDSIDE
Reduction In body weight is an independent risk factor for mortality in chronic heart failure. Insights from GISSI-HF and Val-HeFT trials

P. Rossignol[1], S. Masson[2], S. Barlera[2], A. Castelnovo[2], C. Scardulla[3], G. Tognoni[4], I. Anand[5], J.N. Cohn[6], L. Tavazzi[7], R. Latini[2] on behalf of GISSI-HF and Val-HeFT Investigators.. *[1]Inserm and University Hospital Nancy Clinical Investigation Centre, Vandoeuvre Lès Nancy, France; [2]Istituto Mario Negri Dept Cardiovascular Research, Milano, Italy; [3]Mediterranean Institute for Transplantation and High Specialization Therapies (IsMeTT), Palermo, Italy; [4]Consorzio Mario Negri Sud, S. Maria Imbaro, Italy; [5]Minneapolis VA Medical Center, Minneapolis, United States of America; [6]VA Medical Center affiliated with the University of Minnesota, Minneapolis, United States of America; [7]Maria Cecilia Hospital-GVM Care and Research, Ettore Sansavini Health Science Foundation, Cotignola, Italy*

Purpose: Earlier studies have shown an association between loss in body weight (LBW) and survival. In this study we evaluate the association between LBW and outcomes in two separate and large recent cohorts of patients with chronic HF, adjusting for estimates of fluid congestion.
Methods: Body weight and estimated plasma volume changes (using the Strauss Formula based on Hb and hematocrit variations) were serially recorded in the GISSI-HF (n= 6975 patients) and Val-HeFT trials (n= 5010). In both studies, patients with at least one episode of LBW $\geq$ 5% during the first year of follow-up were considered as experiencing wasting. In GISSI-HF, self-reported unintentional LBW $\geq$ 2 kg between two consecutive clinical visits within 1 year was also considered. The association between LBW and clinical characteristics or mortality was tested by multivariable logistic or Cox models, as appropriate.
Results: LBW occurred in 16.4% and 15.7% of the patients enrolled in GISSI-HF and Val-HeFT, respectively (unintentional LBW$\geq$ 2 kg in 18.9% in GISSI-HF). LBW was independently associated with the severity of HF (i.e. lower ejection fraction, third heart sound, edema, circulating concentrations of NT-proBNP (the latter assessed in 1200 patients in GISSI-HF, 4200 in Val-HeFT), as well as C-reactive protein or pentraxin 3, assessed in a biomarker substudy, other clinical variables (higher BMI in both studies, higher glucose or COPD in Val-HeFT), but not with plasma volume changes over time. In multivariable analyses adjusting for a number of baseline covariates as well as for plasma volume changes, LBW was an independent predictor of mortality, adverse cardiovascular and non cardiovascular outcomes (Table).

	GISSI-HF LBW ≥5% Adjusted HR (95% CI), p value	GISSI-HF Unintentional LBW ≥2 kg Adjusted HR (95% CI), p value	VAL-HeFT LBW ≥5% Adjusted HR (95% CI), p value
All-cause mortality* (1874 in Gissi-HF, 907 in Val-HeFT)	1.195 (1.051, 1.359) p=0.007	1.215 (1.077, 1.370) p=0.002	1.299 (1.102, 1.531) p=0.002
Cardiovascular death* (1394 in Gissi-HF, 785 in Val-HeFT)	1.226 (1.059, 1.419) p=0.007	1.167 (1.015, 1.341) p=0.03	1.260 (1.005, 1.442) p=0.04
Non-Cardiovascular Death* (410 in Gissi-HF, 115 in Val-HeFT)	1.188 (0.928, 1.521) p=0.17	1.384 (1.074, 1.783) p=0.01	2.122 (1.419, 3.174) p=0.0003

*Unknown cause of death: 70 in GISSI-HF, 7 in Val-HeFT.

Conclusions: Loss in body weight was frequently seen in these large recent

HF cohorts. LBW appears to be multifactorial and independently associated with several adverse outcomes, including non-CV death.

P1527 | BEDSIDE
Co-morbidities in long term prognosis in patients with acute heart failure

S. Petrovic Nagorni, S. Ciric Zdravkovic, D. Stanojevic, R. Jankovic Tomasevic, V. Atanaskovic, V. Topic, M. Pavlovic, L. Todorovic. *Clinic for Cardiovascular Diseases, Nis, Serbia*

Introduction and purpose: Acute heart failure (AHF) is the term used to describe the rapid onset of, or change in, symptoms and signs of HF. In most cases, AHF arises as a result of deterioration in patients with a previous diagnosis of HF. Prognosis in acute heart failure depends on numerous factors. In our prospective study we investigated the influence of the most frequent co-morbidities on 1 year prognosis in patients with AHF.
Methods and results: In our prospective study we included 603 consecutive patients (60.7% men) with AHF treated in Intensive Care Unit. The average age was 71.5±10.4 years. 29.9% had acute coronary syndrome, 27.9% dilatative cardiomyopathy, 23.9% arterial hypertension and 18.4% valvular disease as an etiology factor for HF. 66.7% of patients had HF with reduced LVEF (37.4±13.7%), the average duration of HF was 1.7±1.1 years. Cardiovascular comorbidities: arterial hypertension (80.6%) and atrial fibrillation (47.3%) were the most frequent. The most prevalent non-cardiovascular comorbidities were diabetes (54.7%), chronic renal failure (CRF: 43.3%), acute infections (32.8%), anaemia (26.4%), chronic obstructive pulmonary disease (COPD: 23.9%), depression (10%), hypothyreosis (8%), hyperthyreosis (7.5%), stroke (7.5%) and alcoholism (5.5%). The majority of patients had > 1 co-morbidity (32.8% patients had 3 and 31.8% had 2 associated comorbidities). Arterial hypertension, atrial fibrillation and CRF were most frequently associated. During 1 year follow up mortality was admittedly high: 42.8% (10% died in hospital, 12.9% during 6 months after hospital discharge and 19.9% until the end of follow up period). Logistic regression analysis included all relevant factors (age, gender, echocardiographic, clinical, biohumoral parameters) and co-morbidities. We found that higher mortality rate was associated with alcoholism (13.1 fold increase), COPD (5.52 fold increase), CRF (5.1 fold increase) and the number of co-morbidities (5.07 fold increase) as well as with female gender, low LVEF and NYHA class. Co-morbidities did not have influence on in-hospital mortality.
Conclusion: In our study we found that majority AHF patients had 3 jointed (non)cardiovascular comorbidities which were associated with significantly higher mortality after hospital discharge. Meticulous diagnosis and treatment of all co-morbidities should be the routine part of clinical evaluation in AHF since it could improve long-term prognosis. However it seems that we are far from its practical implementation.

P1528 | BEDSIDE
Low ejection fraction is associated with the history of stroke in Japanese patients with atrial fibrillation: from the Fushimi AF registry

M. Iguchi[1], M. Esato[2], Y.H. Chun[2], H. Tsuji[3], H. Wada[1], K. Hasegawa[1], M. Abe[1], M. Akao[1] on behalf of the Fushimi AF Registry investigators. *[1]Kyoto Medical Center, National Hospital Organization, Kyoto, Japan; [2]Ijinkai Takeda General Hospital, Kyoto, Japan; [3]Tsuji Clinic, Kyoto, Japan*

Purpose: Atrial fibrillation (AF) increases the risks of stroke and death, and the prevalence of AF is increasing significantly (reportedly, 0.6% of total population in Japan). Congestive heart failure (CHF) is considered a risk factor for stroke in patients with AF, and is included in the risk stratification scheme, CHADS2 score, as C factor. However the impact of reduced and preserved left ventricular ejection fraction (EF) on the incidence of stroke is unknown.
Methods: The Fushimi AF Registry, a community-based prospective survey, was designed to enroll all of the AF patients living in Fushimi-ku, Kyoto, which is a typical urban district of Japan with a population of 283,000. At present, we have enrolled 3,378 patients (1.2% of total population) from March 2011 to December 2012. We divided the entire cohort into three groups; CHF with reduced EF (EF<40%) (CHFrEF; n=148), CHF with preserved EF (CHFpEF; n=783), and no CHF (NCHF; n=2,447). Mean EF was 35.8±10.8%, 61.5±10.1%, and 65.7±8.9%, respectively.
Results: CHFpEF group was older (CHFrEF, CHFpEF, NCHF; 73.8±11.8, 78.0±10.1, 73.0±10.9 years of age, respectively), and the proportion of female was higher in CHFpEF group (27.7%, 52.6%, 38.0%). The prevalence of hypertension and diabetes were comparable between the three groups, despite that vascular disease (previous myocardial infarction and peripheral artery disease) was higher in CHFrEF group (37.8%, 13.7%, 7.1%; p<0.01). NT-pro BNP levels and New York Heart Association (NYHA) functional class were worse in CHFrEF group (NT-pro BNP: 7062.9±690.7 pg/ml, 2489.4±315.2 pg/ml, 850.3±278.7 pg/ml; p<0.01, the proportion of NYHA 3 or 4: 54.1%, 32.9%, 0.0%; p<0.01). Left ventricular diastolic dimension was significantly higher only in CHFrEF group (54.7±8.9 mm, 46.7±7.0 mm, 45.9±5.7 mm; p<0.01), and left atrial dimension was larger in CHFrEF and CHFpEF groups (46.0±8.0 mm, 46.6±9.5 mm, 42.6±8.0 mm; p<0.01). Both of the CHF groups showed greater CHADS2 score (2.93±1.31, 2.98±1.18, 1.76±1.26; p<0.01), greater CHA2DS2-VASc score (4.38±1.77, 4.56±1.50, 3.01±1.59; p<0.01) and received higher oral anticoagulant prescription (58.1%, 63.6%, 46.0%; p<0.01), but the rate of previous stroke was higher only in CHFrEF group (24.3%, 19.3%, 19.3%).
Conclusion: The Fushimi AF Registry provides a unique snapshot of current real-world AF patients in an urban community in Japan. Low EF but not the history of CHF is associated with the history of stroke in Japanese AF patients.

P1529 | BEDSIDE
Impact of atrial fibrillation on long-term clinical outcomes in heart failure outpatients

H. Kaneko, S. Suzuki, J. Yajima, Y. Oikawa, K. Sagara, T. Otsuka, S. Matsuno, H. Kano, T. Aizawa, T. Yamashita. *The Cardiovascular Institute, Tokyo, Japan*

Purpose: Atrial fibrillation (AF) is a common arrhythmia in patients with heart failure (HF). Recently, several reports revealed that AF was not associated with adverse long-term clinical outcomes of hospitalized HF patients. However, the impact of AF in unselected HF outpatients on long-term clinical outcomes remained unclear. In the present study, we aimed to clarify the impact of AF on clinical outcomes among Japanese HF outpatients in real-world clinical practice.
Methods: With a single hospital-based cohort in the Shinken Database 2004-2011, comprising all the new patients (n=17517) visiting the Cardiovascular Institute Hospital, we followed 2024 outpatients who were diagnosed as having symptomatic HF at the initial visit.
Results: AF was observed in 310 patients (15%). Patients with AF were older, and more likely to be female, more likely to have a lower rate of obesity, hypertension, dyslipidemia, diabetes mellitus, ischemic heart disease, whereas, had a higher rate of anemia, chronic kidney disease, valvular heart disease, dilated cardiomyopathy and prior history of stroke. Averaged BNP in patients with AF was significantly higher than that in patients without AF. AF group had a lower prevalence of NYHA II, whereas a higher prevalence of NYHA III and IV heart failure than Non-AF group. Patients using beta-blockers, renin-angiotensin-system inhibitors, diuretics, digitalis, anti-arrhythmic drugs, and warfarin were more common in patients with AF. Left ventricular ejection fraction was lower in patients with AF than those without. Cox regression analysis showed that AF was associated with higher incidence of all-cause death (p=0.015, hazard ratio (HR) 1.631, 95% confidence interval (CI) 1.099-2.420), cardiovascular death (p=0.009, HR 2.022, 95% CI 1.196-3.420), and HF admission (p<0.001, HR 3.107, 95% CI 2.286-4.224). The Cox regression model used in the analysis adjusted for the covariates showed that patients with AF had a comparable risk for all-cause death (p=0.115, HR 0.573, 95% CI 0.286-1.146), HF death (p=0.608, HR 0.690, 95% CI 0.167-2.844), and cardiovascular death (p=0.564, HR 0.772, 95% CI 0.320-1.861), whereas had significantly higher risk for HF admission (p=0.007, HR 1.781, 95% CI 1.172-2.704). Sub analysis showed that the clinical impact of AF on HF outpatients might be stronger in patients with female, younger age, ischemic etiology, preserved EF, and mild HF symptom.
Conclusions; Among unselected HF outpatients, AF was commonly observed. AF was not associated with long-term mortality, but independently associated with HF admission in HF outpatients.

P1530 | SPOTLIGHT 2013
Does renal function influence the prognostic impact of type 2 diabetes mellitus in patients with chronic heart failure and reduced left ventricular ejection fraction?

G. Russo[1], G. Cioffi[2], L. Tarantini[3], A. Cherubini[1], G. Faganello[1], C. Mazzone[1], G. Barbati[1], R. Candido[4], G. Boscutti[5], A. Di Lenarda[1]. *[1]A.S.S. n 1, Cardiovascular Center, Trieste, Italy; [2]Villa Bianca Hospital, Trento, Italy; [3]San Martino Hospital, Belluno, Italy; [4]A.S.S. n 1, Diabetology, Trieste, Italy; [5]University Hospital "Riuniti", Department of Nephrology, Trieste, Italy*

Preface: Type 2 diabetes mellitus (T2DM) frequently co-exists and is a strong prognosticator of adverse outcome in chronic heart failure (CHF). Both T2DM and CHF are associated with renal dysfunction, a condition named cardio-renal syndrome which heavily influences the clinical management of CHF patients. In this study we tested the hypothesis that the degree of renal dysfunction has a significant influence on the prognostic role of T2DM in patients with CHF and reduced left ventricular ejection fraction (LVEF).
Methods: From November 1, 2009 to December 31, 2012, the "Trieste Registry of CV Diseases" enrolled 19589 patients with CV ambulatory evaluation. Clinical data were derived from the E-data chart for outpatient clinic (Cardionet®) of CV Center of Trieste, Italy, and collected in a regional Data Warehouse. Data on patients with a diagnosis of CHF and reduced LVEF (defined as values of LVEF < 50%) were analyzed. The primary end-point was all-cause mortality.
Results: 554 patients were selected (73±10 years old, 32% females), 192 had T2DM (35%). During a follow-up period of 23±11 months, 115 patients died (21%), 38 of them (7%) within the first year of observation. All-cause death occurred in 57 of 192 patients (30%) who had T2DM and in 58 of 362 (16%, p<0.001) patients who had not. Considering the total study population, Cox regression analysis revealed that T2DM was associated with an increased risk of death (adjusted HR 2.55 [95% CI 1.02-6.36], p=0.04) independently of NYHA class, serum sodium, no therapy with ACEi/ARB, no therapy with beta-blocker. However, when patients were grouped according to the absence or presence of renal dysfunction [defined as glomerular filtration rate (eGFR) <60 ml/min·1.73m^2