

P1801 Impact of temporal changes in left ventricular ejection fraction in patients at risk for heart failure

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Background: We have recently demonstrated that left ventricular ejection fraction (LVEF) dynamically changes and affects prognosis of patients with heart failure (HF).

Purpose: To examine temporal changes in LVEF and their clinical impacts in patients at risk for HF.

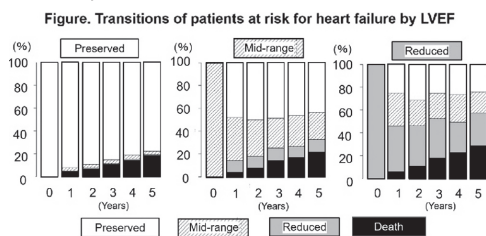
Methods: In our CHART-2 Study, we divided 4,943 consecutive cardiovascular patients at risk for HF into 3 groups by baseline LVEF (Preserved, $\geq 50\%$, N=4,494; Mid-range, 40–49%, N=304; Reduced, $<40\%$, N=145). Transitions among the 3 groups from baseline to 1-year were examined in relation with prognosis.

Results: Mid-range and Reduced at registration dynamically transitioned to other groups at 1-year, whereas Preserved did not (Figure); at 1-year, Mid-range transitioned to Preserved and Reduced by 48% and 10%, respectively, and Reduced transitioned to Preserved and Mid-range by 25% and 29%, respectively, whereas Preserved transitioned to Mid-range and Reduced only by 2.9% and 0.5%, respectively. Transitions from Preserved to Mid-range (adjusted hazard ratio (aHR) 1.8, 95% CI 1.1–3.0, P=0.03), Preserved to Reduced (aHR 2.5, 95% CI 1.0–6.3, P=0.05), and Mid-range to Reduced (aHR 2.6, 95% CI 1.2–6.0, P=0.03) were significantly associated with increased 5-year mortality. Transitions from Preserved to Reduced (aHR 4.7; 95% CI 1.4–15.5, P=0.01), and Mid-range to Reduced (aHR 3.4, 95% CI 1.2–9.6, P=0.02) were significantly associated with increased 5-year HF hospitalization, whereas transitions from Mid-range or Reduced to Preserved were not. The linear regression analysis showed that each group had different sets of factors related to LVEF changes, but left ventricular (LV) dilatation was associated with LVEF decrease in all groups (Table).

Factors related to LVEF changes

	Preserved			Mid-range			Reduced		
	Coef	95% CI	P-value	Coef	95% CI	P-value	Coef	95% CI	P-value
LVDd	-1.1	-1.5 to -0.7	<0.001	-5.0	-6.8 to -3.3	<0.001	-7.0	-9.9 to -4.1	<0.001
BMI				0.5	0.1 to 0.9	0.016			
HHD							8.9	1.1 to 16.8	0.027
BNP				1.4	0.2 to 2.6	0.025			
CcB				4.2	1.3 to 7.1	0.004			

BMI, body mass index; BNP, B-type natriuretic peptide; CcB, calcium antagonist; coef, coefficient; HHD, hypertensive heart disease; LVDd, left ventricular end-diastolic diameter; LVEF, Left ventricular ejection fraction.



Conclusions: Among asymptomatic patients at risk for HF, temporal decrease in LVEF was significantly associated with worse outcomes, suggesting the importance to maintain LVEF to ameliorate long-term prognosis of this population.

P1802 Frequency of recovery and relapse in patients with nonischemic dilated cardiomyopathy on medical therapy

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Background: With advances in medical and device therapy, complete recovery of the normal left ventricular systolic function (LVSF) is seen with increasing frequency. However, the clinical variables associated with such dramatic improvement of ventricular performance are poorly defined. Additionally, a common dilemma that arises in patients whose LVSF normalizes with standard medical therapy is whether they must continue medical treatment indefinitely or whether treatment can be safely discontinued.

Objectives: We evaluate the frequency and predictors of recovery and relapse in patients with dilated cardiomyopathy.

Methods: One thousand seventy-eight patients (n=1078) of a nonischemic dilated cardiomyopathy cohort having baseline left ventricular ejection fraction (LVEF) $\leq 40\%$ were divided into 3 groups: improved group with sustained recovery of LVEF to $\geq 40\%$ with a net increase in LVEF of $\geq 5\%$ from baseline, not-improved group with no change or decrease in LVEF compared with that in baseline includ-

ing patients with an increase in LVEF $<5\%$, and relapsed group with decrease in LVEF $\geq 5\%$ after initial improvement. Patients with significant coronary artery disease were excluded. Follow-up duration was 48 ± 41 months.

Results: The cohort of 1078 patients was 42% female with a mean age of 55 ± 14 years. At entry, 90% were receiving angiotensin-converting enzyme inhibitors or angiotensin receptor blockers and 75% were receiving beta-blockers, which increased to 97% and 88% at 6 months. Five hundred seven patients (47%) did not improve. Of the 571 patients (53%) who improved, 345 (62%) had sustained improvement. Remaining 275 (38%) of the 478 improved patients relapsed on further follow-up. Baseline LVEF was similar in the 3 groups [LVEF of $27.5 \pm 6.9\%$ at initial presentation]. No significant difference among the groups with or without recurrent heart failure was observed in the baseline clinical and echocardiographic characteristics. However, more patients in the recurrent dilated cardiomyopathy group than those in the group that maintained the recovery state had discontinued antiheart failure medication (82.5% versus 10.9%, $P < 0.01$).

Conclusions: With currently recommended medical therapy, 1/3 of patients with nonischemic DCMP have sustained improvement, and $> 1/3$ of those who improve relapse. The recurrence was significantly correlated with the discontinuation of antiheart failure drugs.

P1803 Biomarkers in heart failure patients with and without diabetes

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Introduction: Heart failure patients with type 2 diabetes have an even worse prognosis than heart failure patients without diabetes. The explanation for this excess risk is uncertain and does not seem to be fully explained by the greater prevalence of coronary artery disease and renal dysfunction in individuals with diabetes. We have measured an array of biomarkers to gain insight to potential additional pathophysiological processes active in heart failure patients with diabetes compared to those without.

Methods: We measured a panel of biomarkers reflecting a range of pathophysiological processes in the Controlled Rosuvastatin Multinational Trial in Heart Failure trial (CORONA) which enrolled patients with HFrEF of ischaemic aetiology.

Results: Levels of many biomarkers were higher in patients with diabetes compared to those without, including those reflecting myocyte stress/injury such as high-sensitivity (hs) troponin T (median [IQR] 16.5 [8.5, 32.5] vs 13.0 [6.0, 23.2] pg/ml, $P = 0.0001$) and biomarkers reflecting inflammation e.g. hs CRP (4.0 [1.8, 8.2] vs 3.3 [1.5, 7.2] mg/L, $P = 0.0001$) [Table]

Table 1. Biomarker levels according to history of diabetes

	Patients, n (%)	No diabetes	Diabetes	P-values
Myocyte stress/injury				
NTproBNP (pmol/L)	3664 (73)	172.2 [72.0, 363.3]	177.7 [75.6, 377.1]	0.3519
ST2 (ng/mL)	1449 (29)	17.6 [12.8, 24.6]	18.8 [13.7, 25.6]	0.0285
Troponin T (pg/mL)	1245 (25)	13.0 [6.0, 23.2]	16.5 [8.5, 32.5]	0.0001
Inflammation				
hsCRP (mg/L)	4961 (99)	3.3 [1.5, 7.2]	4.0 [1.8, 8.2]	0.0001
IL6 (pg/mL)	1480 (30)	2.9 [1.8, 5.3]	3.2 [1.9, 5.8]	0.0852
TNF- α (ng/mL)	1480 (30)	3.7 [3.7, 3.7]	3.7 [3.7, 3.7]	0.1071
ECM remodeling				
Galectin-3 (ng/mL)	1462 (29)	18.8 [15.4, 23.7]	19.6 [15.8, 23.9]	0.0739
Endostatin (ng/mL)	1391 (28)	154.5 [124.3, 195.6]	160.4 [129.9, 209.5]	0.0211
IGFBP7 (ng/mL)	1442 (29)	54.2 [45.7, 65.1]	57.0 [47.9, 69.7]	0.001
Kidney function				
NGAL (ng/mL)	1415 (28)	296.0 [215.0, 431.0]	302.0 [209.5, 453.5]	0.8651
Creatinine (μ mol/L)	5011 (100)	110.5 [97.0, 128.5]	110.5 [97.0, 133.0]	0.0011

Conclusions: Biomarkers reflecting myocyte stress/injury, inflammation and remodelling were higher in HF patients with diabetes. It is possible that these differences contribute to the worse outcomes in HF patients with diabetes.

P1804 The added value of exercise stress echocardiography in heart failure patients: the role of dual evaluation of cardiac index and pulmonary congestion

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Background: Doppler echocardiography can provide reliable and repeatable measures of cardiac index (CI), whereas lung ultrasound (LUS) represents a novel, quantitative approach to assessment of pulmonary congestion. In ambulatory HF patients, exercise stress echocardiography (ESE) may endow with hemodynamic information that can allow us to classify patients into hemodynamic categories with different risk.

Aim: Our study tested the hypothesis that simultaneous ESE assessment of CI and LUS is valuable to define categories of HF outpatients with different risks of adverse outcome.

Methods and results: Standard transthoracic and LUS evaluation were assessed during semi-supine ESE in 105 NYHA class I-III HF patients (86 males; age 67 ± 11 years) with reduced left ventricular ejection fraction ($30 \pm 7\%$). CI and B-lines were measured at baseline and at peak stress. Resting plasma BNP levels were also evaluated. Patients were classified into four profiles: A), peak CI ≥ 3.5 l/min/m² and stress-B lines ≤ 15 (no evidence of congestion or hypoperfusion, n=55); B), peak CI < 3.5 l/min/m² and stress-B lines ≤ 15 and (hypoperfusion without congestion, n=14); C), peak CI ≥ 3.5 l/min/m² and stress-B lines > 15 (congestion with adequate perfusion, n=20); and D), peak CI < 3.5 l/min/m² and stress-B lines > 15 (congestion and hypoperfusion, n=16). There were 18 deaths and 19 hospitalization for worsening HF during a median follow-up of 27 months. Combination of stress-induced B-lines at LUS and CI < 3.5 l/min/m² (D profile) was the most powerful independent predictor of death or hospitalization for worsening HF (Odds Ratio [OR]: 4.46; p=0.0002) followed by BNP levels (OR: 1.00; p=0.02). 36-month event-free survival at Kaplan-Meier estimates showed that prognosis was worse in patients with D profile (13%) followed by patients with C (71%), B (75%) and A (83%) profiles (log-rank: 57.5; p<0.0001).

Conclusion: Dual evaluation of CI and LUS during ESE is useful to risk stratify patients with chronic HF and reduced ejection fraction. Evidence of pulmonary congestion and low CI at peak stress identifies a subgroup with a very high risk of adverse outcome.

P1805

Risk stratification in heart-failure-patients with EF <35% during waiting with usage of the WCD in 203 patients - Recovery depending on age and baseline ejection fraction

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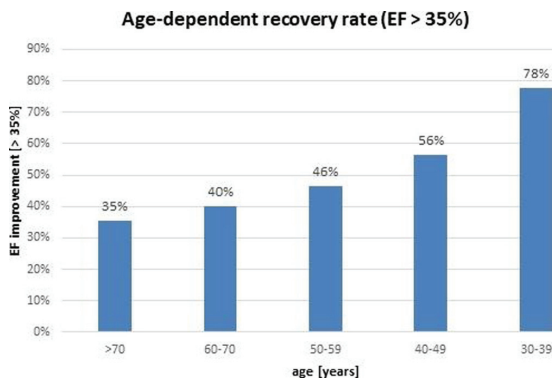
Introduction: Whilst a reduced ejection fraction (EF) is clearly an indication for the implantation of an ICD, the results of randomized trials and current guidelines demand a waiting period in which the patient might recover and is no longer indicated for an ICD. During this period of Guideline directed medical therapy (GDMT) the patient is at high risk for sudden cardiac death (SCD). The wearable cardioverter defibrillator (WCD) allows us to discharge those patients knowing that they will be protected by a noninvasive, reversible method. During this time the patients can be followed up and arrhythmic events will be recorded and deliver additional parameter to support the decision for further treatment strategy. The correlation between such parameters as patient age or the baseline EF, and the rate of recovery is still unclear.

Methodology: Based on the recommendations of the HRS and the hospital own screening protocol we prescribed a WCD for patients with an EF of 35% and lower. During the GDMT-period patients were monitored by the device-own telemonitoring system. Patients were divided in an ICM and NICM group. Age, ejection fraction upon admission and after three months were analyzed.

Results: 203 Patients with LVEF <35% have been fitted with the WCD. The median wear-time was 23,6 h/d SD ± 4.7 . Patients were divided in an ICM and NICM group. In the total cohort 100 pts (49%) did not show EF improvement above ($\leq 35\%$), hence the decision was made to implant an ICD/CRT-D. Whilst in the ICM - group 16 patients (30%) did not need an ICD, 68 patients (53%) in the NICM-group did not have criteria for an ICD.

The patients showed an age- dependent improvement of ejection fraction. In the group of patients aged from 30–39 years 78% showed EF-Improvement $> 35\%$. Despite the fact that in the older population the recovery is lower, still 35% of patients aged > 70 experienced recovery and did not need an ICD/CRT-D. The older the patients, the more unlikely was a recovery to an EF $> 35\%$. A correlation between baseline EF and recovery rate could not be shown.

Summary: The usage of the wearable cardioverter defibrillator in combination with the hospital own screening protocol supported in determining heartfailure patients for an ICD. When patients were reevaluated a significant number did not need an ICD after the waiting period due to significant improvement of the ejection fraction.



Age dependent recovery rates

Data show a clear age-dependent improvement in ejection fraction. A dependency on baseline EF could not be shown.

P1806

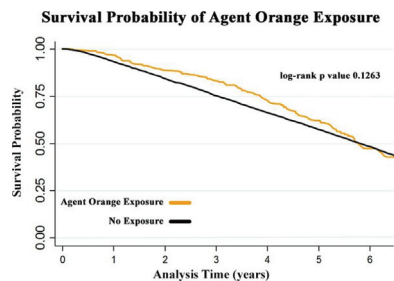
Agent Orange exposure in veterans with heart failure

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Background: Agent Orange was a tactical herbicide used from 1962 to 1975 by the U.S. military. The U.S. Department of Veterans Affairs (VA) compensates veterans for Agent Orange exposure and are offered to receive benefits. The relative impact of Agent Orange exposure on patients with heart failure with reduced ejection fraction (HFrEF) remains unclear.

Methods: The VA's national database was queried to identify all patients diagnosed with HFrEF from 2007 to 2015. Patients were identified with HFrEF through ICD-9 codes and concomitant use of beta blocker through VA outpatient pharmacy. Patients who died within 30 days of the initial HF diagnosis were excluded. Mortality data was collected through the VA's death registry. We compared characteristics of HFrEF patients with and without Agent Orange exposure. We matched patients with Agent Orange exposure using propensity score matching techniques after adjusting for sex, comorbidities, and medications. We analyzed the mortality outcomes through Kaplan Meier survival curves and Cox proportional Hazard model.

Results: We identified total 114,010 veterans with HFrEF and found 391 patients with Agent Orange exposure. The mean age was similar between Agent Orange exposure (68 years vs 67 years). Patients with Agent Orange exposure have a higher rate of coronary artery disease (73% vs 64%), COPD (49% vs 32%), hypertension (74% vs 66%), PAD (30% vs 24%), and OSA (24% vs 17%; p<0.01 for all variables). After controlling for all the covariates on the matched sample, the veterans with Agent Orange exposure had better survival than those without exposure. The Cox proportional hazard model adjusted for covariates on matched sample shows HR of 0.64 (p<0.001; 95% CI = 0.50 to 0.80).



Kaplan-Meier survival estimates of Agent

Conclusions: Veterans who were exposed to Agent Orange have a higher burden of comorbidities however survival estimates were similar. After matching for comorbidities the veterans with HFrEF who were exposed to Agent Orange had decreased mortality.

P1807

Left atrial function in heart failure with mid-range ejection fraction differs from that of heart failure with preserved ejection fraction: a two-dimensional speckle tracking echocardiographic study

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Background: Heart failure (HF) with mid-range ejection fraction (HFmrEF), a newly defined category by the recent ESC HF guidelines, shares similar diagnostic criteria with HF with preserved ejection fraction (HFpEF) including diastolic dysfunction (DD) and structural dysfunction such as left atrial (LA) enlargement. Whether LA function differs between HFmrEF and HFpEF is unknown.

Objectives: To compare LA phasic function in HFmrEF and HFpEF patients using two-dimensional speckle tracking echocardiography (2D-STE).

Methods: Consecutive outpatients from HF clinics fulfilling current recommendations were enrolled prospectively. All patients underwent echocardiography including 2D-STE. We included 110 HFpEF and 61 HFmrEF patients, and 37 healthy controls matched by age. Patients with non-sinus rhythm, significant valve disease, implantable pacemakers, or suboptimal image quality were excluded. Taking the onset of QRS complex as a reference point, peak-atrial longitudinal strain (PALS), peak-atrial contraction strain (PACS), and PALS-PACS were measured reflecting LA reservoir, pump and conduit function, respectively. Global PALS and PACS were obtained from 12 LA segments from the apical four- and two-chamber views. Data are mean [95% confidence interval].

Results: Among HF groups, conventional echocardiographic measures of left ventricular (LV) diastolic function (E/A, e', E/e', tricuspid regurgitation velocity and DD grades), and LA volume (39.5 ± 13 ml/m² in HFmrEF vs. 38.8 ± 12.7 ml/m² in HFpEF) were similar. Both HF groups had abnormal LA phasic function compared to controls (all p<0.001). Overall, HFmrEF patients had worse LA phasic function than HFpEF patients (global PALS 20.6% [19.1, 22.2] vs. 26.2% [24.9, 27.5],