

HR each contributed significantly to the improvement in EF observed with chronic β -blocker treatment. Reverse remodeling (i.e., decreased end-diastolic volume) is not a major factor.

9:00 a.m.

874-3

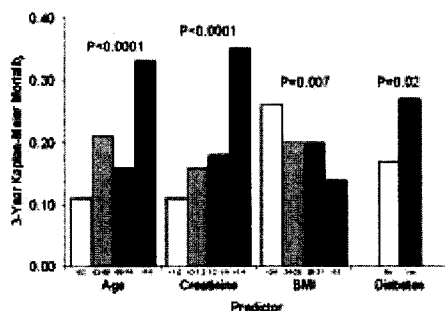
Predictors of Mortality in Patients With Heart Failure and Preserved Systolic Function in the Digitalis Investigation Group Trial

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Background: Although diastolic heart failure is common, the factors that predict mortality have not been clearly defined.

Methods: We studied 988 patients (59% men) with documented heart failure and ejection fraction > 45% who were enrolled and prospectively followed in the Digitalis Investigation Group (DIG) trial. During 3.1 years of follow-up, there were 231 deaths (23%).

Results: The average age was 67 ± 10 years, and the average ejection fraction was $55 \pm 8\%$. There were 285 patients with diabetes (29%) and 557 with ischemic heart disease (57%). In univariable analyses, predictors of death included older age, increasing serum creatinine, decreasing body mass index, and presence of diabetes (Figure shows quartiles or presence of these versus 3-year Kaplan-Meier death rates).



Gender, ejection fraction, and etiology of heart failure were not predictors of death. In stepwise multivariable Cox regression analyses that considered 20 covariates, independent predictors of death were increasing creatinine (score $\chi^2 = 66$, $P < 0.0001$), NYHA class ($\chi^2 = 25$, $P < 0.0001$), recent worsening heart failure ($\chi^2 = 12$, $P = 0.0005$), older age ($\chi^2 = 10$, $P = 0.0017$), body mass index ($\chi^2 = 4$, $P = 0.038$), diabetes ($\chi^2 = 5$, $P = 0.023$), and use of diuretics ($\chi^2 = 4$, $P = 0.038$).

Conclusions: Diastolic heart failure is associated with a high death rate. Important predictors of death include age, renal function, functional class, body mass index, and diabetes.

9:15 a.m.

874-4

Assessment of Long-Term Outcome in a Population at High Risk for Coronary Artery Disease: Mortality Risk Associated With Ejection Fraction Differs Across Resting Nuclear Perfusion Findings

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Background: Resting myocardial perfusion studies assess myocardial viability in patients with heart failure. The sum rest score (SRS), a marker for perfusion abnormality severity at rest, provides independent prognostic information for patients at low to intermediate risk for coronary artery disease (CAD). However, its prognostic role and potential interaction with ejection fraction (EF) in a high risk population are less well defined.

Methods: We examined 3,275 patients at high risk for CAD who underwent cardiac catheterization and nuclear imaging within a six month interval and were followed up to 8 years. We used Cox proportional hazards modeling to assess the relationship between EF and SRS after adjusting for significant clinical characteristics.

Results: A significant interaction ($p=0.030$) was found between the nuclear SRS and EF. Each 10% decrease in EF for patients with a low risk SRS of 1 provided a 29% increase in mortality risk ($p=0.001$, hazard ratio (HR) =1.29, 95% confidence interval (CI) 1.19-1.40), while those with a high risk SRS of 6 (cohort 75th percentile) had a 37% increase ($p=0.001$, HR 1.37, 95% CI 1.23-1.52). Adjusted survival estimates across SRS levels and EF groups were observed (see table).

Conclusion: Resting perfusion studies significantly impact the interpretation of mortality risk associated with changes in resting EF. This clinical interaction should be taken into account when nuclear perfusion imaging is performed to assess prognosis and viability in the low EF population.

Adjusted Estimates of Percentage Surviving

Patient Groups	1 yr	3 yr	5 yr
EF ≤ 35 , SRS ≤ 15	94.3	83.3	71.9
EF ≤ 35 , SRS > 15	93.7	77.1	58.1
EF >35, SRS ≤ 15	96.5	89.7	81.3
EF >35, SRS > 15	96.3	85.8	80.0

9:30 a.m.

874-5

Improvement in Global and Segmental Left Ventricular Contractility Following Autologous Bone Marrow Cell Transplantation in Humans With Severe Ischemic Heart Failure

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Background: Limited treatment options exist for pts with end-stage ischemic heart failure (HF) not amenable to revascularization. We evaluated the effect of transcatheterial (TE) delivery of autologous bone marrow mononuclear cells (BMNC) in pts with severe HF.

Methods: Ten pts (58 ± 11 yrs, 7 males) with severe LV dysfunction (EF $19 \pm 10\%$) and were included. Bone marrow (50ml) was aspirated and BMNCs were isolated. TE injections were performed using the Myo-Star catheter (NOGA, Biosense) to target hibernating myocardium guided by electromechanical mapping (EMM). Pts were evaluated by a) angiography (LVEF) b) EMM (mean values of linear local shortening (LLS) and unipolar voltage (UniV)) and c) echo (wall motion score index). LVEF and treated vs. non-treated segments were analyzed before and 16 wks after the procedure. Student's paired T-test was utilized.

Results: On angiography LVEF increased from $19 \pm 9\%$ to $24 \pm 12\%$ ($p=0.005$). A total of 18 myocardial segments were injected (2 ± 0.7 per pt). On EMM the mean LLS values in the treated areas increased from $5.7 \pm 3.7\%$ to $10.8 \pm 3.5\%$ ($p=0.005$). UniV values of the treated segments did not vary significantly after cell therapy (from 10.5 ± 3.5 to 10.3 ± 2.7 mV; $p=0.6$).

By echocardiography the wall motion score index decreased from 2.0 ± 0.7 to 1.6 ± 0.6 ($p=0.0005$) in the treated segments and from 1.9 ± 0.3 to 1.7 ± 0.2 ($p=0.01$) in the non-treated segments.

Conclusion: In this small number of pts there was an overall improvement in LVEF by angiography following TE injection of BMNC at 16wk follow-up. There was improvement in segmental contractility in the treated areas by both echocardiographic and EMM criteria. Future studies are needed to further clarify the role of stem-cell therapy in the treatment of severe HF.

9:45 a.m.

874-6

The Association of Left Ventricular Ejection Fraction, Mortality, and Cause of Death in Stable Patients With Heart Failure

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Background: Left ventricular ejection fraction (LVEF) is used as a predictor of prognosis in heart failure (HF) patients, but the manner in which the association of LVEF, mortality, and cause of death varies across the full spectrum of LVEF is incompletely understood.

Methods and Results: We examined the association of LVEF and outcomes in 7788 patients enrolled in the Digitalis Investigation Group trial. With mean follow-up of 37 months, mortality was substantial in all LVEF groups (range LVEFs 15%: 51.7%; >55%: 23.5%). Among patients with LVEFs $\leq 45\%$, mortality rates decreased in a near linear fashion across successively higher LVEF groups (LVEFs 15%: 51.7%; LVEF 36-45%: 25.6%; $P < 0.001$), but mortality was comparable in LVEF groups above 45% (LVEF 46-55%: 23.3%, LVEF >55%: 23.5%; $P=0.25$). In multivariable analysis, the magnitude of the association was reduced (LVEFs $\leq 15\%$: HR 1.84, CI 1.54-2.18; 16-25%: HR 1.47, CI 1.30-1.65; 26-35%: HR 1.13, CI 1.01-1.26; 36-45%: referent; 46-55%: HR 0.91, CI 0.76-1.09; >55%: HR 0.89, CI 0.71-1.10). Patients with lower LVEF were at increased risk of death due to arrhythmia and worsening HF, but these were leading causes of death in all LVEF groups.

Conclusions: Annual mortality was more than 5.5% in all LVEF groups, but lower LVEF