284

Stratification of mortality by risk scores from the EPHESUS trial reveals significant interaction between left ventricular ejection fraction and Killip class

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Purpose: The EPHESUS trial demonstrated that aldosterone blockade with eplerenone significantly decreased risk of all-cause mortality and CV death in post- AMI patients with HF by 15% (P = 0.008) and 17% (P = 0.005), respectively. This post hoc analysis of the EPHESUS trial explored trends in mortality data by baseline LVEF and Killip class.

Methods: 6632 patients with signs and symptoms of CHF post-AMI with LVSD (EF < 40%) were randomized to receive eplerenone or placebo plus standard therapy. The trial continued until 1012 deaths occurred (mean follow-up = 16 months). The primary endpoint was all-cause mortality and the composite of time to CV mortality or CV hospitalization. Subjects were stratified based on baseline LVEF and Killip class. Cox regression analyses with treatment (eplerenone vs placebo), Killip class, and LVEF as explanatory variables in the model, as well as interaction of Killip class and LVEF were performed.

Results: Risk of all-cause death was 71% higher in subjects with LVEF <30% vs those with LVEF $\geq30\%$. Risk of all cause death was 85% higher in subjects in Killip Class III/IV vs those in Killip Class I/II. There were statistically significant interactions between Killip class and LVEF for all-cause mortality and CV mortality. Cox regression analysis revealed that mortality risk in patients with Killip class I/II doubled when LVEF was <30% vs LVEF $\geq30\%$ (P <0.001). However, among patients in Killip class III/IV mortality risk increased 20% (P = 0.129) when LVEF was <30% vs LVEF $\geq30\%$.

Summary of all cause death by baseline Killip Class and LVEF

Covariate	Cox Proportional Hazards Model		
	Hazard Ratio	95% CI	P value
Killip class III/IV (N = 1298)			
vs I/II (N = 5279)	1.851	(1.620, 2.115)	< 0.001
LVEF $<$ 30 (N = 1394)			
$vs \ge 30 (N = 5182)$	1.708	(1.495, 1.950)	< 0.001
Killip I/II LVEF (<30 [N = 1015]			
$vs \ge 30 [N = 263])$	2.043	(1.742, 2.395)	< 0.001
Killip III/IV LVEF ($<$ 30 [N = 379]			
$vs \ge 30 [N = 919])$	1.198	(0.948, 1.514)	0.129

Conclusions: In EPHESUS, Killip class III/IV was associated with higher mortality than Class I/II, regardless of LVEF. However in Killip class I/II, those with LVEF < 30% had a significantly higher mortality rate vs those with LVEF $\geq 30\%$, suggesting the importance of determining Killip Class and LVEF in these patients.

285

Preliminary report on the effects of ultrafiltration in severe heart failure: the Continuous Ultrafiltration for cOngestive heaRt failurE (CUORE) trial

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CUORE is an italian multicenter randomized study aimed at analyzing the efficacy of ultrafiltration (UF) vs conventional pharmacological treatment (Conv) in patients with chronic severe heart failure (HF) who presented to emergency department for HF worsening and weight gain

>4 kg. Patients will be followed up for 1 year. In case of further acute decompensation events, patients will be treated again as assigned at the study enrolment. The present is a preliminary report on the first 21 patients enrolled at December 20, 2007. Ten patients were randomly assigned to UF and 11 to Conv. Patients characteristics were: age 73±8 yrs (UF) and 70±10 yrs (Conv), LVEF 32±7% (UF) and 31±8% (Conv), BNP 1348±1148 pg/ml (UF) and 1004±623 pg/ml (Conv). Clinical stabilization, defined as absence of clinical signs of fluid retention with oral treatment since at least 3 days, was reached in 6.3±4.5 days and 9.1±2.3 days in UF and Conv, respectively (p<0.05). At discharge (first hospitalization) reduction in body weight was -7.7±4.3 kg (UF) and -7.0±3.5 kg (Conv) (p=NS), serum creatinine changed by -0.2±0.6 mg/dl (UF) and +0.0±0.3 mg/dl (Conv) (p=NS), BNP by -467±533 pg/ml (UF) and -428 \pm 389 pg/ml (Conv) (p=NS), plasma Na $^+$ by -0.4 \pm 2.8 mEq/l (UF) and $+1.6\pm3.4$ mEq/l (Conv) (p=NS). Mean follow up was 141 ± 126 days (UF) and 190±121 days (Conv). 1 patient died in the UF group and 3 in the Conv group. Combined events (death and rehospitalization because of HF) were 4 and 13 in UF and Conv, respectively (p<0.1). This preliminary observation shows that in chronic HF and severe fluid retention UF allows to reach same body weight and BNP reduction as Conv treatment with no difference in kidney function. However, clinical stabilization is reached in a shorter time (as an average 3 days less). Furthermore, the number of clinical events in the follow-up (death and re-hospitalization because of worsening HF worsening) shows a positive trend in UF group.

286

De novo acute heart failure and acutely decompensated chronic heart failure: one single syndrome or two different entities?

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Patients (Pts) with acute heart failure (AHF) may present with acutely decompensated chronic heart failure (ADCHF) or de novo HF. The differences between these two clinical presentations are not clear. We have compared clinical characteristics and outcome of ADCHF and de novo HF in 497 consecutive Pts admitted for AHF.

307 Pts (62%) had ADCHF and 190 (38%) had de novo HF. Compared to Pts with de novo HF, those with ADCHF were more likely to have atrial fibrillation (42% vs 27%; p=0.002) and less likely to have a history of hypertension (47% vs 57%; p=0.03). CAD was present in 59% and 50% of Pts, respectively (p=0.07). Patients with ADCHF also had more severe symptoms (NYHA class, 3.6 \pm 0.5 vs 3.4 \pm 0.5 on admission and 2.1 \pm 0.7 vs 1.9 \pm 0.7 at discharge), lower systolic blood pressure (122 \pm 26 vs 132 \pm 27 on admission and 109 \pm 19 vs 117 \pm 18 mmhg at discharge), higher BUN (79 \pm 45 vs 66 \pm 40 on admission and 84 \pm 46 vs 72 \pm 42 gm/l at discharge) (all p<0.01), lower s-sodium (138 \pm 4 vs 139 \pm 3 meq/l; p=0.003), and LVEF (31 \pm 13% vs 36 \pm 14%; p<0.0001) and were more likely to have LV dilatation (82% vs 69% of patients; p=0.001) and medium to severe mitral regurgitation (55% vs 38%; p=0.0003). Length



Figure 1