ORAL CONTRIBUTIONS

802 Heart Failure Prognostic Factors/ Outcomes I

Monday, March 18, 2002, 9:15 a.m.-10:30 a.m.
Georgia World Congress Center, Hall D1

9:15 a.m.

802-1 Elaboration and Validation of a Prognostic Classification for Severe Chronic Heart Failure: Data From EPICAL and RALES Studies

François Alla, Serge Briançon, Faiez Zannad, *INSERM-CHU, Nancy, France.*

The clinical management of severe congestive heart failure (CHF) should be graded according to prognosis in each individual patient. The aim of our study was to elaborate and validate a survival prognostic score for patients with severe CHF, based on readily available clinical variables.
Methods: The EPICAL database provided the score elaboration sample (observational, community-based study - 417 patients, NYHA III/IV, LVEF <30%, 5 years follow-up) ; RALES provided the independent validation sample (clinical trial, spironolactone vs. placebo - sub-sample of 261 patients, NYHA III/IV, LVEF <35%, 2 years follow-up). Baseline variables were tested in Cox multivariate models. The score was defined in the form of linear combinations of the variables included in the model.
Results: Two-years survival rates were 61% in both groups. Five-year survival was 36% in EPICAL. Seven factors were independently associated with survival rate in the EPICAL sample. From theses variables and respective coefficients, the prognostic score may be calculated for each patient as follows: Score = 4 (age greater than (gt) 60 years) + 3 (duration of causal disease gt 1 year) + 2 (prior heart failure decompensation) + 2 (serum sodium lt 138 µmol/l) + 3 (co-morbidity) + 6 (renal impairment) + 3 (furosemide dose gt 120mg/d). Scores ranged from 0 to 23 ; the higher the score the poorer the survival. With best cutpoints, we have constituted a three classes final score: lt 7 (class I), between 7 and 11 (class II), gt 11 (class III). Two-years survival rates were 87% for class I , 66% for class II and 40% for class III. Five-year survival-rates were 67% for class I, 38% for class II and 13% for class III.
The application of this score in the validation sample, showed no differences between predicted and observed survival: two-years survival-rates were 86% for class I, 59% for class II and 35% for class III (p vs. EPICAL NS).
Conclusion: A simple validated score is able to discriminate among advanced CHF patients with low and high risk of death. It may help to identify patients who should be referred for specialist advice or intensive therapy and to manage transplantation waiting lists. It may also provide a useful tool for clinical trials design and analysis.

9:30 a.m.

802-2 A History of Prior Myocardial Infarction Was Independently Predictive of Mortality but Not of Recurrent Myocardial Infarction or Heart Failure Hospitalization in 5477 Patients With Acute Myocardial Infarction Complicated by Cardiac Failure

Ronnie Willenheimer, Klas Gränsbo, Steven Snapinn, Andrew Coats, for the OPTIMAAL study group, *University Hospital MAS, Malmö, Sweden.*

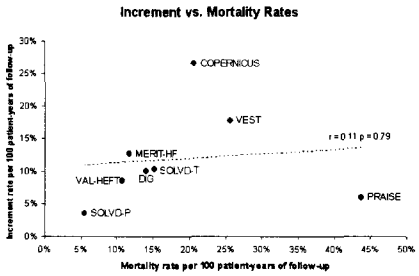
Background: In a large cohort of patients with acute myocardial infarction (AMI) complicated by cardiac failure, we examined any relationship between a history of prior AMI and future morbidity and mortality.
Methods: In 5477 patients with AMI and clinical signs of heart failure (HF) and/or systolic left ventricular dysfunction and/or anterior Q-wave AMI, a history of AMI and 50 other variables comprising demographics, patient history, physical examination, laboratory values and medication were assessed at baseline. Patients were followed-up for a mean of 2.5 years. The value of a history of prior AMI to predict recurrent AMI, HF hospitalization, cardiac death and total mortality was tested in uni- and multivariate analysis using a Cox regression model.
Results: During follow-up there were 657 recurrent AMIs, 625 HF hospitalizations, 403 cardiac deaths and 844 deaths. In univariate analysis a history of prior AMI was significantly predictive of recurrent AMI (HR 1.765, 95 % CI 1.457-2.138, P<0.0001), HF hospitalization (HR 1.695, 95 % CI 1.401-2.051, P<0.0001), cardiac death (HR 2.091, 95 % CI 1.654-2.643, P<0.0001) and all cause mortality (HR 1.904, 95 % CI 1.620-2.237, P<0.0001).
In multivariate analysis, however, a history of AMI was not independently predictive of recurrent AMI or HF hospitalization, but of cardiac death (HR 1.797, 95 % CI 1.418-2.278, P<0.0001) and all cause mortality (HR 1.403, 95 % CI 1.179-1.669, P=0.0001).
Variables independently predictive of recurrent AMI were age (HR 1.025/year, P<0.0001), inclusion based on Q-wave AMI (HR 0.738, P=0.0003), prior Aspirin use (HR 1.617, P<0.0001) and country of residence.
Variables independently predictive of HF hospitalization were age (HR 1.043/year, P<0.0001), pulmonary congestion at X-ray (HR 1.573, P<0.0001), history of diabetes (HR 1.655, P<0.0001), prior diuretic use (HR 1.562, P<0.0001), pulse rate (HR 1.016/beat/min, P<0.0001), serum urea (HR 1.067, P<0.0001), smoking (HR 1.228, P=0.0003), and country of residence.
Conclusion: In a high risk post AMI population a history of AMI was independently predictive of cardiac and all cause mortality, but not of recurrent AMI or HF hospitalization, in this multivariate model.

9:45 a.m.

802-3 Impact of Combining Fatal and Nonfatal Endpoints in Heart Failure Trials

Hicham Skali, Scott D. Solomon, Jacobus Lubsen, Marc A. Pfeffer, *Brigham and Women's Hospital, Boston, Massachusetts, SOCAR Research SA, Nyon, Switzerland.*

Background: In randomized clinical trials (RCT), sample size is often estimated based on a presumed endpoint event rate. Frequently, composite endpoints are constructed to have more events in the population and hence reduce that sample.
Aim: To test the assumption that using a composite endpoint of heart failure (HF) hospitalization (hosp) or death results in a consistent increase in event rate across HF RCTs.
Methods: HF trials were selected if they enrolled more than 1000 patients for a mean follow-up of at least 9 months and if the endpoints evaluated included mortality and a composite endpoint of death or HF hosp. Average duration of the placebo arm follow-up was derived from the mean duration of follow-up in both arms and mortality odds ratio. Placebo event rates per 100 patient-years (pt-yrs) of follow-up for mortality and the composite endpoint were estimated. The Increment was defined as the difference in event rates between the composite endpoint and mortality.
Results: Eight major RCT met the entry criteria. Events rates per 100 pt-yrs of follow-up ranged from 5.5 to 43.7 for death and from 9.1 to 49.7 for the composite endpoint. The increment rate in each trial ranged from 3.5 to 26.6 events per 100 pt-yrs of follow-up. The increment was not correlated with mortality rate (r=0.11, p=0.79).



Conclusion: Although combining HF hosp with death increases event rates, the absolute increment varies widely unrelated to disease severity. In HF RCTs, sample size estimation based on this composite endpoint is unreliable.

10:00 a.m.

802-4 The Impact of Gender on Prognosis in Patients With Advanced Heart Failure

Jalal K. Ghali, Heidi Krause-Steinrauf, Kirkwood F. Adams, Jr., Steven Goldman, Steven S. Khan, Mary A. Peberdy, Yves D. Rosenberg, Clyde W. Yancy, Jr., James B. Young, JoAnn Lindenfeld, *Cardiac Centers of Louisiana, Shreveport, Louisiana.*

We examined the effect of gender on prognosis in the Beta Blocker Evaluation of Survival Trial (BEST), which randomized 2115 men and 593 women with heart failure (NYHA class III or IV with LVEF ≤ 35 %) to bucindolol or placebo. Complete data were available on 579 women and 2049 men. Women were younger (mean age 58 vs 61 years), included more blacks (30% vs 21%), less CAD (36%vs 62%), higher LVEF (25% vs 23%), and similar number of diabetics (36% vs 35%). A multivariate analysis, using Cox proportional hazard regression, was performed to assess the predictive value of several clinical and laboratory variables on prognosis. **Conclusion** In patients with advanced heart failure and impaired LVEF, female gender plays a protective role and is an independent predictor of survival with men having 32% increase in risk of death after adjusting for major variables known to impact prognosis. This finding is relevant in designing clinical trials and assessing the potential role of new management strategies on survival in patients with advanced heart failure.

N = 2628	Events = 838		
Covariate	HR	95% CI	p-value
CAD (CAD vs non CAD)	1.46	1.25-1.71	0.0001
SBP (mm Hg)	0.99	0.99-0.99	0.0001
CTR	1.03	1.02-1.04	0.0001
Age (year)	1.02	1.01-1.02	0.0001
LVEF (<.20 vs >.20)	0.78	0.67-0.91	0.0010
NYHA (IV vs III)	1.42	1.15-1.75	0.0010
Diabetes Mellitus	1.25	1.08-1.45	0.0023
Gender (male vs female)	1.32	1.09-1.59	0.0040
Race (black vs nonblack)	1.24	1.05-1.47	0.0115