After accounting for age, gender, risk factors, medications, coronary history, exercise capacity, chronotropic response, and heart rate recovery, VEA during recovery remained predictive of death (adjusted HR 1.5, 95% CI 1.2-1.8, P<0.0001), but VEA during exercise was not predictive (adjusted HR 1.1, 95% CI 0.9-1.4, P=0.18).**Conclusion:** As we hypothesized, VEA during recovery after exercise predicts mortality, but VEA only during exercise does not.

3:00 p.m.

830FO-5 Exercise-Induced Ventricular Premature Beats Are Associated With Increased Cardiovascular Mortality: The Framingham Heart Study

Ali Morshedi-Meibodi, Jane Evans, Daniel Levy, Martin G. Larson, Ramachandran Vasan, *NHLBI's Framingham Heart Study, Framingham, Massachusetts, Boston University School of Medicine, Boston, Massachusetts.*

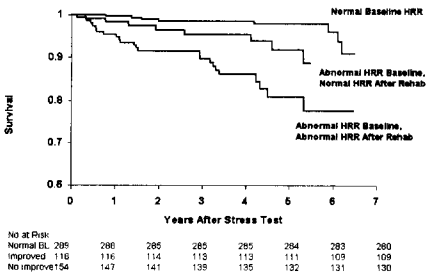
Background: There is controversy regarding the prognostic impact of exercise-induced ventricular premature beats (VPB). While earlier studies reported no adverse relation, the Paris Prospective Study recently reported an increase risk of death in men with exercise-induced VPBs.
Methods: We evaluated 2,840 Framingham Offspring Study subjects (1,388 men, mean age 43 years) who were free of cardiovascular disease and underwent a heart rate-limited exercise test according to the Bruce protocol during a routine examination. 780 subjects (27%) had VPBs during the exercise (median of 0.22 VPBs/minute of exercise). Subjects were divided into three groups based on the numbers of VPBs/minute of exercise: those without any VPBs, those below (low frequency VPBs) and those above the median (high frequency VPBs). Cox proportional hazard regression models incorporating established risk factors (age, sex, diabetes, hypertension, smoking, total and HDL cholesterol) and adjusting for interim cardiovascular disease (CVD) events were used to examine the association of exercise-induced VPBs at the baseline examination with risk of death due to coronary heart disease (CHD), CVD (including CHD and other vascular events), and all-cause mortality on follow up.
Results: On follow up (mean 15 years), 159 subjects died (38 CVD deaths [31 men], 29 CHD deaths [24 men]). Exercise-induced VPBs were associated with increased risk of all-cause mortality [multivariable HR for trend across 3 groups of 1.38, 95% CI, 1.14-1.65], CHD-death [HR 1.82, 95% CI, 1.20-2.74] and CVD-death [HR 1.91, 95% CI, 1.33-2.73]. The high VPB frequency group was associated with the greatest risk of all three outcomes.
Conclusions: In our large community-based sample of men and women, exercise-induced VPBs identified a group at increased risk of death secondary to CHD, CVD, and all-cause mortality. Additional studies are needed to examine the utility of the exercise-induced VPBs for risk stratification.

3:15 p.m.

830FO-6 Heart Rate Recovery Improved in a Cohort of Adults After Cardiac Rehabilitation

Ema Obenza Nishime, Christopher R. Cole, Gregory S. Wallace, Robert J. Rosnick, Claire E. Pothier Snader, Eugene H. Blackstone, Gordon Blackburn, Michael S. Lauer, *Cleveland Clinic Foundation, Cleveland, Ohio.*

Background: An abnormal heart rate recovery after exercise predicts mortality. As exercise modulates autonomic function and heart rate recovery reflects vagal tone, we hypothesized that cardiac rehabilitation would favorably impact heart rate recovery.
Methods: Consecutive adults (n=595, 61±11 years, 78% male) who underwent symptom-limited exercise tests before and after Phase II cardiac rehabilitation were studied. Heart rate recovery (HRR) was the difference of heart rate at peak exercise and one-minute later with ≤ 12 bpm abnormal.
Results: HRR improved from a median of 13 bpm before rehabilitation to 17 bpm afterwards (P<0.0001). There were 287 adults (48%) with abnormal baseline HRR; 161 (56%) were still abnormal afterwards. Predictors of failure to improve HRR included older age (for 10 years, adjusted Odd Ratio [OR] 1.3, 95% CI 1.0-1.7, p=0.03), lesser change in exercise capacity (for 1.5 METs, adjusted OR 1.3, 95% CI 1.1-1.6, p=0.002). During 4 years, there were 42 deaths. After adjusting for age, gender, and change in exercise capacity, abnormal baseline HRR predicted death (12% vs. 3%, adjusted HR 4.0, 95% CI 1.8-8.8, p=0.0006). Failure to improve an abnormal HRR tended to predict higher mortality (adjusted HR 2.0, 95% CI 0.9-4.3, P=0.08) (Figure).



Conclusion: Heart rate recovery improved in patients after cardiac rehabilitation. Although we cannot exclude regression to the mean, the tendency of an improved HRR to predict lower mortality suggests that this was prognostically meaningful.

POSTER SESSION

1133 Myocardial Function/Adrenergic Receptors

Monday, March 18, 2002, 3:00 p.m.-5:00 p.m.
Georgia World Congress Center, Hall G
Presentation Hour: 3:00 p.m.-4:00 p.m.

1133-137 Myocardial Overexpression of the Cardiac b-Adrenergic Receptor Kinase-1 Inhibitor (BARKI) Delay the Development of Cardiomyopathy Induced by Myocardial Expression of Monocyte Chemo-Tactic Protein-1 (MCP-1)

Samer J. Khouri, Philip Binkley, Walter Koch, Pappachan Kolattukudy, *Ohio State University, Columbus, Ohio, Duke University, Durham, North Carolina.*

Background: Targeted expression of MCP-1 in the cardiomyocytes induces cardiomyopathy in a murine model. We hypothesized that overexpression of BARKI in these MCP-1 mice may delay the progression of ventricular remodeling. **Methods:** Studies were performed on mice with targeted myocardial expression of BARKI, MCP-1, BARKI and MCP-1 (MCP-BARKI) and wild-type mice as controls. 2D and M-mode echo were performed at baseline, 1 and 2 month. **Results:** At baseline MCP-1 and MCP-BARKI mice did not have a significant difference in mass 68.4 ± 0.6 & 68.6 ± 0.7 mg nor in EF 42 ± 5 & 44 ± 3 % and they were significantly different from BARKI mice and controls (Figures). The MCP-BARKI and MCP-1 mice increased LV mass to the same extent at one month. However, at two months, the LV mass was significantly greater in the MCP-1 mice as compared to MCP-BARKI mice 92.9 ± 8.3 and 80.0 ± 1.3 mg, respectively. BARKI and control mice had mild increase in cardiac mass, but significantly different from MCP-1 and MCP-BARKI mice 69.9 ± 0.4 and 70.9 ± 1.7, respectively. The EF did not show significant change over time (figure 2). **Conclusion:** βARKI overexpression does not preserve myocardial contractility in mice with cardiomyopathy that express MCP-1, but has a significance effect on the cardiac mass. This suggests a significant influence of BARKI overexpression in preventing cardiac remodeling. This may suggest a novel molecular target for future therapies targeted at the prevention of progressive ventricular remodeling in patients with heart failure.

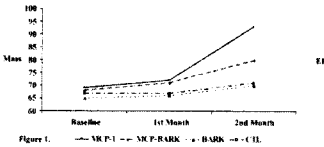


Figure 1.

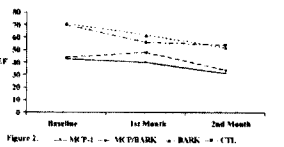


Figure 2.

1133-138 Down-Regulation of Sodium Current in Heart Failure: Rescue by Beta-Blockers

Albertas I. Undrovinas, Victor A. Maltsev, Hani N. Sabbah, *Henry Ford Heart and Vascular Institute, Detroit, Michigan.*

Background: Ion channel remodeling is believed to provide a substrate for ventricular arrhythmias in heart failure (HF). We recently showed that Na^+ channels (NaCh) responsible for excitation generation and propagation in the heart are down-regulated in chronic infarction-induced dog HF model, a feature that suggests possible involvement of these channels in ventricular arrhythmias. While β-blockers (BB) are known to significantly reduce the risk of the ventricular arrhythmias and sudden cardiac death in patients with HF, the cellular and ionic mechanisms of this beneficial effect remain unknown. In this study, we tested the hypothesis that BB prevent NaCh downregulation in chronic HF.
Methods: Studies were performed in cardiomyocytes isolated from dogs with chronic HF produced by multiple sequential intracoronary microembolizations. In addition to marked LV systolic and diastolic dysfunction, dogs with chronic HF also manifests spontaneous ventricular arrhythmias and sudden cardiac death occurs in ~13% of HF animals. To study the effects of BB on the regulation NaCh, HF (LV ejection fraction 28±1%) was produced in 12 dogs. Six HF dogs were treated for 3 months with carvedilol (1 mg/kg, twice daily) and 6 were untreated and served as controls. In addition, cardiomyocytes from 9 normal dogs were used for comparison. At the end of 3 months of therapy, mid-myocardial cardiomyocytes were isolated from the LV free wall. The whole-cell maximum Na^+ current (I_{Na}) was measured using patch-clamp technique in symmetrical Na^+ solutions ($[Na]_i=[Na]_o=5mmol/L$) at room temperature. Chronic treatment with carvedilol restored I_{Na} density in dogs with HF. I_{Na} density in carvedilol dogs was significantly higher compared to that of untreated HF dogs (46.4±0.9 pA/pF vs. 33±3.3 pA/pF, P=0.008) and was similar to that of normal dogs (48.5±5.1 pA/pF). The voltage dependence of steady-state inactivation and activation of I_{Na} remained unchanged in both carvedilol-treated and untreated HF dogs.
Conclusion: Down-regulation of NaCh in ventricular cardiomyocytes caused by chronic HF in dog can be prevented by a chronic therapy with β-blockers.