

VO<sub>2</sub>max (16.3±0.7 vs 18.7±0.8 ml/kg/min, p<0.001). Good correlations were found between training-induced increase in VO<sub>2</sub>max and training-induced reduction in levels of proinflammatory cytokine TNF-α (r=-0.54, p<0.01) and apoptosis inducer sFasL (r=-0.57, p<0.005) in CHF patients. On the contrary, no significant difference in circulating cytokines and apoptotic markers was found with physical training in normal subjects.

**Conclusions:** Physical training reduces plasma levels of proinflammatory cytokines and sFas/sFasL system in patients with CHF. These immunomodulatory effects may be related to the training-induced improvement in functional status of CHF patients.

11:00 a.m.

**856-3 The Oxygen Uptake Efficiency Slope as a Predictor of Mortality in Chronic Heart Failure**

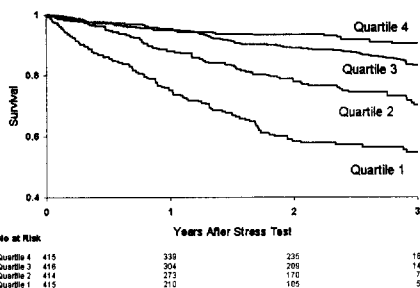
A. Thomas McRae, III, James B. Young, M. Luay Alkotob, Claire E. Pothier Snader, Eugene H. Blackstone, Michael S. Lauer, Cleveland Clinic Foundation, Cleveland, Ohio.

**Background:** The oxygen uptake efficiency slope, defined as V<sub>O2</sub>/log(V<sub>E</sub>), has been proposed as an effort-independent measure of cardiovascular fitness. The prognostic value of oxygen efficiency as compared to maximum V<sub>O2</sub> has not been assessed.

**Methods:** We followed 1661 consecutive patients with chronic heart failure who were referred for metabolic stress testing for heart transplant evaluation. Patients were followed for a median of 2 years (range 0-5 years). Patients who had transplantation (n=190) were censored.

**Results:** Quartile values of oxygen efficiency were 0.98±0.15, 1.31±0.08, 1.60±0.10, and 2.12±0.33. Compared to patients in the highest quartile, those in the lowest quartile had a lower peak V<sub>O2</sub> (10.5 vs. 23.7 ml/kg/min), were older (57 vs. 48 years), and were more likely to have coronary disease (54% vs. 27%). There was a strong association between lower oxygen efficiency and mortality (Figure)

Kaplan Meier Curve of Oxygen Efficiency by Quartiles



(unadjusted hazard ratio [HR] of lowest to highest quartile 6.5, 95% CI 4.5 to 9.3, P<0.0001). In a Cox regression analysis that accounted for demographics, coronary disease, V<sub>E</sub>/V<sub>CO2</sub> slope, and other potential confounders, oxygen efficiency was an independent predictor of death (adjusted HR of lowest to highest quartile 4.1, 95% CI 2.6 to 6.5, P<0.0001), whereas maximum V<sub>O2</sub> was no longer predictive (adjusted HR of lowest to highest quartile of V<sub>O2</sub> 1.2, 95% CI 0.5 to 3.0). **Conclusion:** The oxygen uptake efficiency slope is a strong and independent predictor of mortality in patients with chronic heart failure.

11:15 a.m.

**856-4 Improved Ventilatory Response at Peak Exercise Despite No Change in Peak Oxygen Consumption With Chronic Beta-Blockade in Heart Failure Patients**

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**Background:** Although chronic beta-blockade has been shown to improve resting cardiac function in heart failure patients, there are minimal improvements in exercise capacity as measured by peak oxygen consumption. (PeakVO<sub>2</sub>) Recently, the ventilatory response to exercise, V<sub>E</sub>/VCO<sub>2</sub>, has been shown to have prognostic value in heart failure patients. The effect of beta-blockade on the ventilatory response to exercise is unknown.

**Methods:** 26 patients with non-ischemic cardiomyopathy underwent cardiopulmonary exercise testing prior to and after six months of treatment with either placebo or beta-blockade (carvedilol or metoprolol). Peak exercise heart rate, VO<sub>2</sub>, and V<sub>E</sub>/VCO<sub>2</sub> were compared to baseline in each treatment group.

**Results:**

	Placebo (pre)	Placebo (post)	Beta-Blocker (pre)	Beta-Blocker (post)
LVEF, %	24±2	28±4	20±2	35±2*
Peak HR, bpm	145±4	144±2	145±5	114±4*
Peak VO2 ml/kg/m	17.2±1.6	16.8±1.9	15.4±1.0	15.7±1.0
Peak V <sub>E</sub> /VCO <sub>2</sub>	42.2±2.8	41.0±3.9	45.8±2.2	40.4±1.5*

(\* p < 0.05)

**Conclusion:** Chronic beta-blocker therapy results in a reduction in the excess ventilation with exercise in heart failure patients This reduction in V<sub>E</sub>/VCO<sub>2</sub> may have a favorable effect on both prognosis and functional capacity in heart failure patients.

**856-5**

**Exercise Training Worsens Prognosis of Cardiomyopathic Hamsters (BIO14.6) via Beta<sub>1</sub>-Adrenergic Stimulation**

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**Background.** Although exercise training improves prognosis of ischemic heart failure, the effects on nonischemic heart failure are still unclear even in animal models. Because of metabolic vulnerability to sympathetic stimulation of failing hearts, exercise training may adversely affect the prognosis of nonischemic heart failure despite the beneficial effects on exercise capacity. To test the hypothesis, we examined the effect of exercise training with or without beta-blocker therapy on exercise capacity and prognosis of cardiomyopathic hamsters. **Methods.** We assigned 87 BIO14.6 hamsters at 30 weeks of age into 3 groups; sedentary control group (group C, n=27), exercise training group (group Ex, n=30), and exercise training plus beta-blocker group (group ExB, n=29). On Day 1 of the study, baseline treadmill exercise was performed to determine the maximal running speed at which animals could catch up. On Day 2, exercise training and medication were started. Treadmill exercise for 25 min at 50% of the baseline maximal speed was performed on every week days for 160 days in groups Ex and ExB. In group ExB, metoprolol of 1mg/kg/day, a cardioselective beta<sub>1</sub>-blocker, was orally administered during the study. To assess exercise capacity, the maximal treadmill exercise was performed on Day 30 and Day 90. The survival rate was assessed. **Results.** The maximal treadmill speed gradually decreased in groups C and ExB. However, the initial decrease on Day 30 was not observed in group Ex, suggesting a short-term benefits of exercise training on exercise capacity. In contrast, the survival rate was lower throughout the study in group Ex than in group C (Kaplan-Meier, p<.005). This effect was partly but significantly attenuated in group ExB (p<.005). The survival rate on Day 160 was 70% in group C, 48% in group ExB, and only 33% in group Ex. **Conclusion.** Despite short-term benefits on exercise capacity, exercise training aggravated prognosis of cardiomyopathic hamsters. This effect was attenuated by cardioselective beta<sub>1</sub>-blockade. Our results suggest that long-term exercise training promotes the progression of cardiomyopathy via Beta<sub>1</sub>-adrenergic stimulation.

11:45 a.m.

**856-6**

**Brain Natriuretic Peptide Levels Predict Exercise Capacity in Patients With Chronic Heart Failure**

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**Background:** Plasma levels of brain natriuretic peptide (BNP) are elevated in patients (pts) with chronic heart failure subject to the degree of systolic and diastolic left ventricular dysfunction. Whether BNP levels are likewise associated with exercise capacity in pts with CHF is unknown.

**Methods:** 70 consecutive pts with CHF (60 ± 10 years, 19 women, LVEF 26 ± 4 %) and 10 healthy controls (55 ± 16 years, 4 women, LVEF 59 ± 5 %) referred for cardiopulmonary exercise testing (CPX) were prospectively studied. Resting BNP (pg/ml; immunoassay, Biosite Diagnostics, San Diego, USA) was obtained after 10 minutes of supine rest prior to symptom-limited bicycle exercise CPX.

**Results:** BNP concentrations were significantly higher in pts with CHF than in controls (427.6 ± 377.6 vs. 24.8 ± 22.1 pg/ml, p < 0.0001). In CHF pts BNP levels strongly correlated with oxygen uptake, both at anaerobic threshold (VO<sub>2</sub>AT: r = -0.54, p < 0.001) and maximum exercise (VO<sub>2</sub>max: r = -0.56, p < 0.001). Impairment of ventilatory efficiency (EqCO<sub>2</sub>: r = 0.43, p < 0.001) and maximum exercise level (watts % predicted : r = -0.44, p < 0.05) correlated less well with BNP. There was a significant inverse correlation between LVEF and BNP (r = -0.50, p < 0.05). BNP discriminated well pts with a VO<sub>2</sub>max < 11 ml/min/kg (Area under the ROC 0.80 ± 0.09) with a criterion value of 470 pg/ml. BNP levels > 470 pg/ml were significantly associated with VO<sub>2</sub>max < 11 ml/min/kg (risk ratio 13.1 [95%CI 2.5-69.2])

**Conclusions:** BNP is clearly associated with exercise capacity in CHF. BNP levels show a significant correlation with the impairment of ventilatory efficiency and oxygen uptake at maximum exercise and anaerobic threshold. BNP is able to discriminate between CHF pts with moderately or severely impaired exercise capacity.