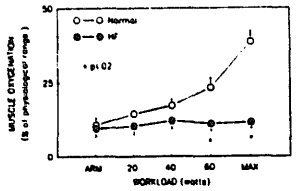
Tuesday, March 5, 1991
2:00PM–3:30PM, Room 215, East Concourse
Mechanisms of Exercise Intolerance in Heart Failure

2:00

SKELETAL MUSCLE UNDERPERFUSION IN HEART FAILURE IS PRODUCED BY EXERCISE-INDUCED MUSCLE VASOCONSTRICTION

John R. Wilson, Donna M. Mancini, Andrea J. Rein, Lynne Georgopoulos, University of Pennsylvania, Philadelphia, PA

In ambulatory patients with heart failure (HF), muscle blood flow is normal during small muscle exercise but reduced during strenuous exercise. To determine why strenuous exercise results in muscle underperfusion, we monitored arterial blood pressure (BP) and forearm hemoglobin-myoglobin oxygenation during forearm exercise (0.4 watts) in 8 patients with HF and 8 normal subjects. Forearm exercise was first performed alone and then with concurrent progressive bicycle exercise. Muscle oxygenation was monitored with near-infrared spectroscopy (760-800 nm absorption) and normalized relative to the total change in oxygenation produced by forearm cuff ischemia (Circulation 80:1668, 1989). Bicycle exercise increased the BP similarly in both groups. However, muscle oxygenation improved in only the normal subjects, indicating that the BP increase in the patients was counteracted by muscle arteriolar vasoconstriction:



These findings suggest that muscle underperfusion during strenuous exercise in patients with heart failure is due to activation of vasoconstrictor influences.

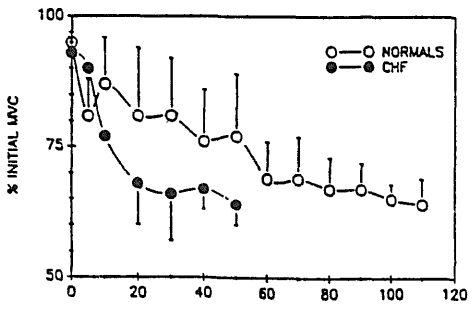
2:15

MUSCLE FUNCTION IN CONGESTIVE HEART FAILURE

Ian Christoph, John Minotti, Roberta Oka, Lauren Wells, Barry Massie. University of California and VAMC, San Francisco, CA.

CHF PTS have abnormal skeletal muscle morphology and metabolism; however, their muscle function has not been well defined. Therefore, we compared quadriceps strength, fatiguability, and endurance in 9 NYHA Class I-IV patients with 5 sedentary, aged-matched controls. Isometric *strength* was defined as the greatest of 3 maximal voluntary isometric contractions (MVC). *Fatigue* was defined as the time for maximal isometric torque to decline by 40% from the initial MVC. Isokinetic *endurance* was quantified as the ratio of the mean torque during the last 3 of 15 quadriceps extensions to the mean torque of the first 3 repetitions at a constant velocity of 180°/sec. Although CHF patients had near normal strength (MVC 93±20 vs 100±30 ft-lbs, p=NS), CHF PTS fatigued significantly faster (Fig.1). Isokinetic endurance was also reduced in CHF PTS, with force declining to 61±18% vs 89±12% of initial (p<.02).

ISOMETRIC FATIGUE



Thus, CHF PTS have increased quadriceps fatiguability and decreased endurance, and these functional changes in muscle may play a role in exercise intolerance.

2:30

Skeletal Muscle Metabolic Abnormalities in Congestive Heart Failure are not due to Muscle Atrophy

Donna M. Mancini, Andrea Rein, Glenn Walter, Nathaniel Reichek, Robert Lenkinski, John R. Wilson, University of Pennsylvania, Philadelphia, PA

Patients with heart failure (HF) exhibit an abnormal skeletal muscle metabolic response to exercise which is not explained by muscle underperfusion. To investigate whether these metabolic abnormalities result from muscle atrophy, we performed ^{31}P magnetic resonance spectroscopy and imaging of the calf in 15 patients with HF (EF=17±6%, peak VO_2=16±5 ml/kg/min) and 10 control subjects (Peak VO_2=33±9 ml/kg/min). Inorganic phosphorus (P_i), phosphocreatine (PCr), and intracellular pH were measured at rest and during plantarflexion at workloads of 0.75 to 6 watts. Muscle volume was obtained from the sum of the integrated area of muscle in 1 cm thick contiguous axial images from the patella to the calcaneus. The work slope i.e. P_i/PCr vs power output, an index of muscle oxidative metabolism, was significantly greater in patients with HF than in control subjects (Normal: 0.25±0.24; HF: 0.89±0.92 $Watt^{-1}$; p<0.05), indicating abnormal oxidative metabolism. Intracellular pH at peak exercise was significantly reduced in patients with HF (HF: Rest 7.01±0.07; Ex: 6.74±0.28; p<0.05) but not in normal subjects (Normal: Rest 7.02±0.03; Ex: 6.93±0.17; NS). Skeletal muscle volume was significantly reduced in patients with heart failure (Normal: 1274±311; HF: 1007±232 cm^3; p<0.05). No significant correlations were observed between the work slope or lowest pH and muscle volume in patients with heart failure, in normal subjects or in the entire group (r≤-0.3; p=NS for all). Though the average work slope in patients with heart failure was 350% greater than that observed in normal subjects, muscle volume was decreased by only 20%. These findings suggest that skeletal muscle metabolic abnormalities in patients with heart failure are not simply a consequence of muscle atrophy. The etiology of these metabolic abnormalities remains unexplained.

2:45

SKELETAL MUSCLE METABOLISM IN EXPERIMENTAL HEART FAILURE: EFFECTS OF INFARCT SIZE AND PHYSICAL TRAINING

Stamatis Adamopoulos, Francois Brunotte, Andrew Coats, David Lindsay, Bheeshma Rajagopalan, George Radda, Peter Sleight, John Radcliffe Hospital, Oxford, UK.

The mechanisms of the skeletal muscle metabolic changes of chronic heart failure are unknown. The influence of myocardial infarction and physical deconditioning on skeletal muscle metabolism was studied by 31P magnetic resonance spectroscopy (MRS) in female Wistar rats 12 weeks after coronary artery ligation (n=21) or sham operation (n=8). Infarcted rats were allocated randomly to either 6 weeks training (n=10, rodent treadmill 15m/min, 30mins/day, 6 days/week) or non-training (n=11). 31P spectra were collected from the calf muscle during sciatic nerve stimulation (1Hz) both supramaximally and submaximally(to produce 200gr tension). Rats were further divided into congestive (C) and non-congestive (NC) groups using lung/body weight ratio as an index of the severity of heart failure. pH was calculated from the chemical shift of inorganic phosphate (Pi) and changes in phosphocreatine (PCr) were expressed as PCr/PCr+Pi.

	Maximal tension		200gr	
	pH	PCr/PCr+Pi	pH	PCr/PCr+Pi
Training NC	6.96±.02	0.54±.07	7.00±.01	0.71±.02
Training C	6.96±.01	0.53±.04	7.01±.01	0.67±.04
Non-training NC	6.96±.01	0.52±.08	6.97±.02	0.72±.04
Non-training C	6.86±.04**	0.40±.06	6.93±.03*	0.49±.06**
Sham	6.96±.04	0.54±.04	6.99±.01	0.71±.04

There was no difference between either training group, sham or NC non-training rats (ANOVA). The C non-training rats produced significantly more lactate and used more PCr compared to all other groups (*=p<0.05, **=p<0.01 ANOVA). PCr/PCr+Pi at maximal tension showed a similar trend but was not significant (p<0.068).
We conclude that the MRS changes (excessive PCr depletion and acidification) in skeletal muscle of chronic heart failure depend on both severity of failure and physical deconditioning; training may prevent these changes.