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823-6 Low Insulin-like Growth factor-I Predicts Wasting, Anabolic Deficiency, Cytokine and Neurohormonal Activation in Chronic Heart Failure

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Background: Acquired abnormalities of biochemical parameters of the growth hormone (GH) - insulin-like growth factor I (IGF-I) axis have been associated with severe chronic heart failure. The clinical and functional status and the degree of cytokine and neurohormonal alteration of CHF patients with low IGF-I levels are unknown.

Methods: Patients with CHF were divided into two groups according to their IGF-I levels (classified according to the lower limit of our and the manufacturer's assay range in normal controls): low IGF-I < 104 (n = 20; 89 ± 2 ng/ml), and normal/high > 104 ng/ml (n = 32; 169 ± 9 ng/ml). Between groups there was no difference in age (low vs high: 65 ± 3 vs 62 ± 2 years, p = 0.21), body mass index, aerobic capacity MVO₂ (low vs high: 15.2 ± 1.2 vs 17.3 ± 1.1 ml/kg/min, p = 0.23), LVEF, NYHA classification.

Results: During quadriceps strength testing, patients with low IGF-I showed less endurance (-26%), absolute strength (-26%), and strength per unit area muscle (-15%) than patients with normal/high IGF-I; DEXA-scan detected an increased fat/muscle ratio (18%). These alterations were accompanied by increased levels of GH (235%), tumor necrosis factor- α (63%), cortisol/dihydrocortisone ratio (89%), noradrenaline (49%), and adrenaline (166%; all at least p < 0.05).

Conclusion: Patients with low IGF-I levels show signs of selective skeletal muscle wasting, cytokine and neuroendocrine activation, as well as anabolic depletion to a greater extent than patients with normal/high levels.

824 New Insights Into Thallium-201

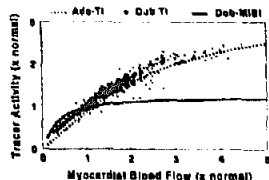
Monday, March 30, 1998, 4:00 p.m.-5:30 p.m.
Georgia World Congress Center, Room 254W

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824-1 Favorable Myocardial Uptake of Thallium-201 During Dobutamine Stress in the Presence of Coronary Artery Stenoses: Implications for Pharmacologic Stress Perfusion Imaging

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Dobutamine (Dob) stress adversely affects the myocardial uptake of sestamibi (MIBI), leading to underestimation of blood flow disparity in the presence of coronary stenoses. To determine if this Dob effect is generalizable to other perfusion tracers, we measured the myocardial uptake of ²⁰¹Tl (TI) during Dob stress in 13 open-chest dogs with LAD stenoses, and compared the Dob TI results to our previous data with adenosine (Ado) TI (n = 13) and Dob MIBI (n = 15) in the same canine models. As expected, Dob (30 μ g/kg/min) increased flow in the stenotic and normal zones to 1.4 and 2.6x resting flows, respectively, resulting in a stenotic:normal flow ratio of 0.47 ± 0.04, similar to our previously reported Dob-induced flow ratio (0.47 ± 0.03), and slightly less than the flow ratio produced with Ado stress (0.32 ± 0.04; P < 0.05). As shown below, TI uptake during Dob closely approximated the TI flow-extraction curve for Ado, and was markedly higher than the flow-extraction curve for MIBI during Dob. Consequently, easily detectable TI defects were present on post-Dob ex vivo imaging (count ratio 0.60 ± 0.03), similar to the TI defects produced by Ado (0.67 ± 0.03) and more severe than the MIBI defects produced by Dob (0.81 ± 0.03) (P < 0.001).



Thus, the myocardial uptake of TI is similar with either Dob or Ado stress, indicating that the adverse effect of Dob on MIBI uptake is not generalizable to TI. These findings suggest that TI might be preferable to MIBI for Dob stress perfusion imaging. A clinical comparison is clearly warranted.

824-2 Clinical and Exercise Variables are Independent Predictors of Survival in Patients With one Abnormal Coronary Territory on Exercise Thallium Images

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Background: Although patients with only 1 abnormal coronary territory (1ACT) on their exercise TI²⁰¹ images are often assumed to have single-vessel coronary artery disease and therefore a benign prognosis, three vessel or left main disease (3VLM) has been reported in 26% of such patients (pts) referred for angiography. A multivariate model was developed in a training population of 264 pts who had 1ACT and angiography. Four clinical and exercise variables—diabetes, hypertension, magnitude of ST segment depression, and exercise rate-pressure product—were found to be independent predictors of 3VLM.

Methods: To test the validity of the training model in pts who were referred for exercise TI²⁰¹ imaging, 495 consecutive pts from a separate cohort with 1ACT (reversible or fixed) were followed for a median duration of 7 years. Follow up was 96% complete. Pts were classified into low, medium, and high risk groups based upon the 4 clinical and exercise variables comprising the training model. Kaplan-Meier estimates of survival free of cardiac death were significantly different (p = 0.0002) between the risk groups:

Risk group	Number	8 yr survival	Cardiac mortality/yr
Low	129	98%	0.3%
Intermediate	270	85%	1.9%
High	96	73%	3.4%

Conclusion: Patients with 1ACT by exercise TI²⁰¹ imaging have divergent outcomes that can be predicted from clinical and exercise variables. Low-risk pts have a prognosis equivalent to that previously reported for patients with normal stress TI²⁰¹ images, whereas high-risk pts have substantial cardiac mortality despite only 1ACT.

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824-3 Histomorphologic Profile Myocardial Segments With Normal Thallium Activity in Chronic Ischemic Cardiomyopathy

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In pts with chronic CAD and LV dysfunction, asynergic segments with normal thallium (TL) activity may show lack of improvement in contractile function after revascularization. Since analysis of TL relies on normalized data, (in which the segment with greatest TL activity is set to 100% and other segments are analyzed relative to this reference standard), we hypothesized that varying degree of interstitial fibrosis may explain the lack of postoperative improvement in such segments. We studied the histomorphologic profile in 13 chronic ischemic cardiomyopathy pts listed for cardiac transplantation who underwent TL SPECT. The explanted hearts were sliced in short-axis sections and the volume fraction of collagen from midventricular slices were studied quantitatively using computerized videodensitometry after staining with picrosinus red. A total of 28 segments were identified to have normal TL activity ($\geq 85\%$ peak), with a mean of 96 ± 6%. The volume fraction of collagen replacement in such segments ranged from 4.4 to 38% (mean 15.0 ± 8.7%) which was significantly higher than the mean volume fraction of collagen obtained in 13 age-matched normal hearts without CAD (mean 4.1 ± 1.7%, p < 0.001). The distribution of collagen replacement among the CAD pts was due to a combination of interstitial fibrosis (n = 27) and subendocardial (n = 10) or diffuse (n = 5) microscopic infarcts. In addition, despite exhibiting normal TL activity, 12 of the 14 segments with >15% collagen volume were supplied by severely narrowed coronary arteries. These histomorphologic data provide a potential explanation for the apparent discrepancy between degree of viability by TL and recovery of function after revascularization in such pts.

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824-4 Obtaining Optimum and Consistent SPEW Myocardial Counts Using an Anterior Planar View to Determine SPECT Acquisition Times

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Background: Prior studies have demonstrated large variability in count density and therefore image quality in TI-201 myocardial perfusion SPECT images using standard protocols. This study explores using the myocardial