1141-62 Effect of Tetrahydrobiopterin on Coronary Microcirculation in Healthy and Hypercholesterolemic Subjects

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Background: Tetrahydrobiopterin (BH4) is an essential co-factor of the NO-synthase, which regulates vasomotion. It has been shown to normalize endothelial dysfunction in the forearm of hypercholesterolemic patients. br />Aim: To determine the acute effect of intravenous BH4 on myocardial blood flow (MBF) in hypercholesterolemic patients and in healthy controls at rest as well as during endothelial-dependent (exercise) and -independent (adenosine, Ado) hyperemia.

Methods: 15O-labelled H2O and PET was used to measure regional MBF (ml/min/g) at rest, during Ado (0.14mg/kg/min over 7 min) and immediately after supine bicycle exercise in 10 healthy male volunteers with normal cholesterol levels (mean workload 199 Watts, 105 % predicted) and in 8 hypercholesterolemic subjects (102 Watts, 71 % predicted). Both groups had no history of and low clinical probability for CAD. Sixty minutes later all MBF measurements were repeated after intravenous BH4-infusion (10mg/kg over 30 min).

Results: Resting MBF and Ado-induced hyperemic MBF are not significantly affected by intravenous BH4. Exercise induced hyperemic MBF increases significantly ($p<0.05$) after BH4 in both groups.

Conclusions: In healthy men as well as in hypercholesterolemic patients, BH4 increases the endothelial-dependent hyperemic response to bicycle exercise, but not the endothelial-independent response to Ado. This provides evidence for a role of BH4 in the regulation of coronary microcirculation during physical exercise.

flow values are given in ml/min/g

	Controls			Hypercholesterolemics		
	Rest	Ado	Ex	Rest	Ado	Ex
Baseline	1.33 ± 0.42	4.52 ± 1.10	2.96 ± 0.58	1.48 ± 0.18	4.69 ± 1.15	2.61 ± 0.74
BH4	1.38 ± 0.37	4.85 ± 0.45	3.41 ± 0.73	1.43 ± 0.28	4.53 ± 0.93	2.82 ± 0.69
p	ns	ns	<0.05	ns	ns	<0.05

1141-63 Detection and Reproducibility of Mental Stress Induced Ischemia Utilizing Tc-99m Sestamibi Single-Photon Emission Tomography in Normal and Coronary Artery Disease Population

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Background: Mental stress induced ischemia, as detected by equilibrium radionuclide angiography studies, has yielded reversible ischemia in only 30-60% of patients with exercise induced ischemia. The purpose of this study was to evaluate the sensitivity and reproducibility of mental stress induced ischemia in patients with coronary artery disease (CAD) and in normal controls (with a low likelihood of CAD) using sestamibi single-photon emission tomography (SPECT) imaging.

Methods: 15 patients with CAD and typical angina or reversible ischemia (positive exercise treadmill study or positive adenosine thallium study) and 21 normal controls underwent mental stress testing (public speaking task.) Myocardial perfusion imaging was performed at peak stress (one minute) and compared to rest images obtained on a separate day. Images were read by 2 experienced readers using a 20 segment model scored on a scale of 0-3 for severity. Ischemia was defined as new or worsening perfusion defects with mental stress as compared to resting baseline images. Conflicting scores were resolved by consensus. Reproducibility was evaluated with repeated mental stress testing and nuclear imaging performed an average of two weeks later.

Results: 10 of the 15 patients (67%) with CAD demonstrated ischemia with mental stress as detected by sestamibi SPECT imaging. The mean number of perfusion defects attributable to mental stress was 4.1 with a mean severity of 2.54. Of the 10 patients with ischemia on the first test, all were reproducible on the second. None of the 21 normal controls had evidence of mental stress induced myocardial ischemia.

Conclusion: In patients with known CAD with typical angina or with evidence of reversible ischemia, mental stress was effective in inducing myocardial ischemia by sestamibi SPECT imaging in 67% of the patients studied. With repeated mental stress testing and nuclear imaging, these findings also demonstrated high reproducibility. In all 21 normal controls, mental stress did not induce myocardial ischemia. Further studies are indicated to explore the role of mental stress nuclear imaging in patients with CAD.

1141-64 Sestamibi Perfusion Imaging Predicts Wall Motion Recovery Beyond TIMI Grade 3 Flow Following Primary Stenting

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Background: The improvement in wall motion abnormalities following myocardial infarction (MI) depends on complete tissue level reperfusion. Preserved metabolism identified with sestamibi perfusion imaging in dysfunctional myocardial segments may predict wall motion recovery (WMR).

Objectives: 1) To assess the improvement in wall motion abnormalities among MI patients treated with primary stenting and final TIMI 3 flow; 2) To assess the role of quantitative sestamibi SPECT to predict WMR in the infarcted myocardium.

Methods: We prospectively enrolled MI patients with less than 12 hours of symptoms and TIMI 3 grade flow post primary stenting. All patients were injected with sestamibi immediately after PCI and imaged with SPECT. WMR was assessed comparing two echocardiogram performed upon admission and at 6 weeks. We calculated specificity, sensitivity, positive predictive value, negative predictive value of preserved tracer activity (>50% of peak activity) to predict WMR.

Results: A total of 312 myocardial segments were evaluated in 24 patients. Motion abnormalities were present in 109 segments. We observed WMR in 68 (62%) and no improvement in 41 (38%). The table displays the predictive information of preserved tracer activity.

Sensitiviy	95% (95% CI 86 - 99)	Positive Predictive Value	78% (95% CI 67 - 87)
Specificity	61% (95% CI 45 - 75)	Negative Predictive Value	90% (95% CI 72 - 97)

Conclusions: Among MI patients treated with primary stenting and TIMI 3 grade flow, a substantial proportion of dysfunctional myocardial segments do not improve at 6 weeks. Our findings suggest that a tissue level reperfusion marker, such as sestamibi, predicts WMR.

1141-65 Improved Quantification of Tc-99m Sestamibi Myocardial Perfusion Attenuation Corrected SPECT Imaging

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Background: Photon absorption, Compton scatter and resolution effects are physical phenomena that can produce imaging artifacts that may lead to misdiagnosis. Previously we developed a correction methodology (ExSPECT II) to compensate for these problems and documented its diagnostic advantage for visual interpretation. The purpose of this investigation is to document whether this correction methodology can also improve quantitative analysis for the detection and localization of CAD.

Methods: 43 patients (29 males, 14 females), 28 who had undergone coronary arteriography and 15 with low likelihood of CAD were imaged using a one-day, rest-stress Tc-99m sestamibi SPECT protocol. These studies were processed twice. The first time using conventional reconstruction and gender-specific quantification. The second time using the correction methodology which incorporates iterative reconstruction of both the emission and transmission (Bayesian) studies and comparison to a single gender-combined, attenuation-corrected normal database. The corrected and uncorrected studies were compared for their accuracy to detect CAD and localize it to the LAD, LCX, and RCA vascular territories.

Results: The conventional quantification of the uncorrected studies yielded the following accuracy: CAD 91% (39/43), LAD 72% (31/43), LCX 79% (34/43), and RCA 81% (35/43). The gender-combined quantification of the corrected studies yielded the following accuracy: CAD 93% (40/43), LAD 72% (31/43), LCX 77% (33/43), and RCA 86% (37/43).

Conclusion: Quantification of attenuation corrected Tc-99m sestamibi myocardial perfusion SPECT studies demonstrated a trend towards improved detection and localization of CAD over quantification of uncorrected SPECT studies.

1141-66 Evaluation of Peripheral Blood Flow During Exercise: A Complement to Exercise Myocardial Perfusion SPECT for Prognostic Assessment

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Background: Coronary artery disease (CAD) patients (pts) often manifest a paradoxical reduction in finger pulsewave amplitude (PWA) during exercise (EX). Since the clinical significance of this finding is unknown, we compared EX PWA responses to a sensitive measure of functional disease severity: summed reversibility score (SRS) on EX Tc-99 Sestamibi myocardial perfusion SPECT.

Methods: 126 CAD pts (mean age 61± 11 years, 89% male) had PWA assessed by peripheral arterial tonometry (PAT) during EX SPECT. PWA for each minute of EX was compared as a ratio to the rest value. A 5 point score (0 = normal uptake, 4 = absent uptake) was assigned to 20 SPECT segments to determine SRS. 55 additional pts (mean age 53 ± 10 years, 51% male) with a low likelihood (LL) of CAD (<5%) were used as a referent group.

Results: The mean slope of PWA response was positive among the LL pts but negative in the CAD pts (11 ± 109 vs -57 ± 167, p=0.006). When grouped accoding to PWA ratios, CAD pts with the lowest PWA ratio had the highest number of ischemic SPECT studies, more reversible defects and higher SRS (table). Abnormal PWA responses were also associated with lower peak heart rates ($p < 0.05$) and higher peak systolic and diastolic pressures ($p < 0.05$ for each).

Conclusions: Paradoxical falls in peripheral blood flow during EX are associated with a greater frequency and magnitude of EX-induced SPECT hypoperfusion. These data suggest that peripheral arterial tonometry represents a non-invasive method of identifying pts with functionally severe CAD.

PARAMETERS	HIGHEST PWA RATIO PTS	MIDDLE PWA RATIO PTS	LOWEST PWA RATIO PTS	p VALUE
ISCHEMIC SPECT (%)	19.1%	42.9%	61.9%	< 0.001
NUMBER OF REVERSIBLE DEFECTS	0.4 ± 0.7	1.6 ± 2.4	2.8 ± 4	< 0.001
SUMMED DEFECT REVERSIBILTY SCORE	1.5 ± 2.2	4.7± 6	8.8 ± 10.8	< 0.001