POSTER SESSION II
SATURDAY, OCTOBER 2, 2004, 4:00–5:30PM

65.01

DEVELOPMENT OF LIPOSOMES WITH AFFINITY TO ISCHEMIC MYOCARDIUM

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Background: A major impediment to drug diagnosis and therapy of myocardial infarction is the limited access that drugs have to ischemic myocardium, dependent on regional myocardial blood flow. Investigators report that some liposomes concentrate in the experimental myocardial infarction, suggesting that they may be used to transport drugs to a region of ischemia. One of the most promising approaches for increasing liposome circulation time is coating them with polyethyleneglycol (PEG).

Methodology: Unilamellar PEG-coated neutrally charged and positive non-PEG liposomes, both labelled with ^{99m}Tc, were produced. A rabbit myocardial ischemia-reperfusion model was created in which a silk ligature was reversibly tied around the left anterior descending coronary artery (LAD). After 90 minutes of ischemia LAD ligature was untied, ^{99m}Tc-liposomes were injected in the rabbit model, and we followed their distribution during the next 3 hours with gamma camera imaging (dynamic, static and spet acquisitions). ^{201}Tl was simultaneously injected and we also followed its distribution/redistribution through the next 3 hours. After *in vivo* cyntigraphic study, the isolated heart was placed on the gamma camera so a static and a spet acquisition could be made. Tissue samples were obtained from the 3 myocardial regions (nonischemic, viable and infarcted) as well as from other organs of interest for biodistribution study following a standard scheme.

Results/conclusions: A functional and reproductible rabbit myocardial ischemia-reperfusion model was successfully created. Neutral PEG-coated liposomes have higher *in vitro* and *in vivo* stability than positive non-PEG. On *in vivo* images, ^{201}TI redistribution areas which correspond to viable myocardium match the areas of higher ^{99m}Tc-liposome concentration either neutral-PEG and positive non-PEG. Biodistribution study confirmed important cardiac radioactivity with higher relative values in ischemic myocardium than in normal myocardium.

65.02

RISK STRATIFICATION AFTER MYOCARDIAL INFARCTION BY STRESS 99M TECHNETIUM TETROFOSMIN SPECT. IMPACT OF SCINTIGRAPHIC EXTENT OF CORONARY ARTERY DISEASE

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Background. To assess the incremental prognostic value the of stress 99m technetium tetrofosmin myocardial perfusion imaging in patients with previous myocardial infarction.

Methods. We studied 383 patients (age 60 ± 11 year, 280 men) >3 month after acute myocardial infarction by exercise bicycle or dobutamine (up to 40 μg/kg/min) stress 99m technetium tetrofosmin myocardial perfusion tomography. Stress images were acquired 1 hour after stress, and rest images were acquired 24 hours after stress test. An abnormal study was defined as reversible or fixed perfusion abnormality. Myocardial segments were assigned to corresponding coronary arteries as follows: the apex, anterior wall and anterior septum to the left anterior descending coronary artery, the posterolateral wall to the left circumflex, and the posterior septum and the inferior wall to the right coronary artery.

Results. During a follow up of 4.3 ± 2.1 years, 48 cardiac events occurred (36 cardiac deaths and 12 non-fatal myocardial infarctions). Myocardial perfusion was normal in 51 patients, abnormal in single vessel distribution in 170 patients and abnormal in multivessel distribution in 162 patients. The annual cardiac event rates in these groups were 0.4%, 2.6%, and 4% respectively. Survival curves are shown in figure. In a multivariate analysis of clinical data, independent predictors of cardiac events were diabetes mellitus (odds ratio [OR] 2.3, 95% confidence intervals [CI] 1.2–4.5), history of congestive heart failure (OR 2.7, CI 1.4–4) and smoking (2.7, CI 1.5–5). The extent of coronary artery disease on tetrofosmin scans was incremental to clinical data in the prediction of cardiac events (OR 4.8, CI 1.5–9). Model Chi^{2}increased from 18 to 26 ($p<0.01$).

Conclusion. Stress 99m technetium tetrofosmin myocardial perfusion imaging provides incremental prognostic information for the risk stratification of patients with previous myocardial infarction. Event rate is directly related to the scintigraphic extent of coronary artery disease. Patients with normal perfusion have excellent event free survival.

65.03

DIFFERENTIAL IMPACT OF PARASYMPATHETIC WITHDRAWAL TO MENTAL STRESS ISCHEMIA AS ASSESSED BY NONINVASIVE EVALUATION OF MYOCARDIAL PERFUSION AND/OR FUNCTION

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Background: Mentally stressful tasks produce myocardial ischemia in patients with chronic coronary artery disease (CAD) and changes in autonomic response have been implicated in its pathogenesis. The aim of this study was to determine whether MS-induced myocardial ischemia (MSI) assessed by concurrent non-invasive imaging of perfusion and/or function is associated with parasympathetic withdrawal.

Methods: In 19 pts with chronic CAD, we performed simultaneous SPECT MPI, HRV analysis, and echocardiography (echo) at baseline and during MS. MS was performed using a mental arithmetic task. MSI was defined as MS-induced MPI defects and/or regional LV dysfunction by echo. HRV was quantified using spectral analysis.

Results: Eleven (58%) of 19 pts had evidence of MS induced myocardial ischemia (8 MPI defects, 4 wall motion abnormalities by echo). High frequency (HF) power decreased significantly in those patients with MS-induced ischemia but did not change in those without MS-ischemia (see table below)

	HF Baseline (Ln msec^2)	HF MS (Ln msec^2)
MS ischemia (n = 11)	4.36 ± 0.32	3.75 ± 0.26*
No MS ischemia (n = 9)	4.68 ± 0.38	4.97 ± 0.31

(*$p < 0.05$, MS-induced ischemia vs. No MS-induced ischemia)

Among pts with MS ischemia, the greatest decrement in HF was observed in pts with MS-induced SPECT defects compared to those with MS-induced regional LV dysfunction. Patients with MS ischemia had a greater increase in rate-pressure product during MS than those without ischemia (58+20% vs. 34+20% increase, $p<0.05$).

Conclusion: Patients with MS-induced myocardial ischemia during MPI and/or echo show evidence of greater parasympathetic withdrawal. The association of parasympathetic withdrawal to MSI defined by SPECT was more robust than MSI defined by echocardiogram. Future studies using MPI are warranted to determine the precise role of sympathovagal balance in individual patients susceptible to MS ischemia.

65.04

EVALUATION OF CARDIAC HYPERTHROPY IN SPONTANEOUS HYPERTENSIVE RATS USING MEASURES OF LEFT VENTRICULAR DEFORMATION AND LVEF OF CARDIAC MICROPET IMAGING DATA

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