11:15 a.m.

817-2 Prognostic Value of Stress-Induced Ischemia Versus Rest Redistribution Thallium-201 SPECT
Tal Shahar, Daniel S. Berman, Jeroen Bax, John D. Friedman, Sean Hayes, Guido Germano, Cedars-Sinai Medical Center, Los Angeles, California.

Background: The prognostic value of stress-induced ischemia versus viability by rest redistribution thallium-201 has not been evaluated.

Methods: We identified 828 patients who underwent rest and 24-h stress Tc-99m sestamibi SPECT (247 treadmill and 381 adenosine) and also 381-144 hour delayed rest Tc-201 imaging because of resting perfusion defects. Patients were followed up for 2.1±0.7 years. Follow-up time was censored at the occurrence of cardiac death, myocardial infarction or revascularization. Perfusion images were scored using a 20-segment model and a 0-4 scale (0=normal, 4=anterior wall ischemic event) and the summed stress-rest difference score (SRD, amount of stress induced ischemia) and rest-late difference score (RLD, amount of rest redistribution) were derived.

Results: During follow-up 45 cardiac deaths, 25 non-fatal myocardial infarctions and 55 late revascularizations (~90 days after the nuclear test) occurred. Multivariate Cox regression analysis demonstrated that after adjusting for clinical data and for the amount of perfusion abnormality at rest, the SRD was a significant predictor of the combined end point of cardiac death, myocardial infarction and late revascularization (p<0.007), whereas the RLD was non-significant (p=0.1). In predicting myocardial infarction and late revascularization (ischemic events or worsening of coronary disease) SRD was the only significant predictor (p=0.001) of all clinical and perfusion variables. In predicting cardiac death RLD was significant (p=0.004), whereas SRD was non-significant (p=0.8).

Conclusion: In patients with resting perfusion defects, the amount of stress-induced ischemia is a significant predictor of non-fatal ischemic events, whereas the amount of viability is a significant predictor of cardiac death.

11:30 a.m.

818-5 Transfection of Plasmid DNA in Cardiac and Skeletal Muscle With Ultrasound and Intravenous Cationic Microbubble Vehicles
Jonathan P. Christiansen, Alexander L. Klibanov, Jonathan R. Lindner, University of Virginia, Charlottesville, Virginia.

Background: Ultrasound can disrupt microbubbles bearing plasmid DNA may offer a safe, non-invasive method for gene transfer. We investigated the transfection efficiency of ultrasound and intravenously administered cationic microbubbles bearing plasmid DNA to both cardiac and skeletal muscle, and the potential mechanisms for this delivery.

Methods: Plasmid DNA containing a luciferase reporter gene driven by a CMV promoter was charge-coupled to cationic microbubbles. In 5 rats 1 x 10^8 microbubbles pre-incubated with 10μg plasmid were infused into a femoral vein over 3 min. High-power imaging (MI >1.5) at a pulsing interval (PI) of 7 s of both the heart and left hindlimb adductor muscles was performed simultaneously. Luciferase activity, quantified as relative light units (RLU), was analyzed in homogenized tissue 96 hours later. In 5 mice intravital ultrasound destruction of microbubbles bearing luciferase DNA remained bound to the microbubbles during their transit through the microcirculation. Following ultrasound, deposits of DNA were observed in the tissue surrounding intact arterioles and capillaries. Vascular rupture or hemorrhage was rare. The location of fluorescent DNA was visually assessed and recorded for offline analysis.

Results: Transfection was observed in both cardiac and skeletal muscle and was significantly higher in the former (84±26 vs 52±16 RLU, p<0.05). Tissue outside the ultrasound exposure did not receive luciferase. The ultrasound exposure, fluorescence DNA remained bound to the microbubbles during their transit through the microcirculation. Following ultrasound, deposits of DNA were observed in the tissue surrounding intact arterioles and capillaries. Vascular rupture or hemorrhage was rare. Perivascular deposits of DNA were not seen in control mice.

Conclusions: Site-specific transfection of cardiac and skeletal muscle is possible with ultrasound disruption of intravenously administered cationic microbubbles bearing plasmid DNA. DNA remains bound to the microbubbles during their circulation, and is deposited in the perivascular tissue by ultrasound without vessel rupture.

ORAL CONTRIBUTIONS

817 Assessing Outcomes With Nuclear Imaging
Monday, March 18, 2002, 11:00 a.m.-12:15 p.m.
Georgia World Congress Center, Room 256W

11:00 a.m.

817-1 Prognostic Significance of Ischemic Electrocardiographic Changes During Adenosine Infusion in Patients With Normal Myocardial Perfusion Imaging
Maryann Alshag, Brian G. Abbott, Alan K. Berger, Fran J. Wackers, Yale University School of Medicine, New Haven, Connecticut.

Background: Previous studies have demonstrated that patients with normal Adenosine myocardial perfusion imaging (MPI) have a very favorable short-term prognosis (risk of death and myocardial infarction <1% per year). The development of ST-segment depressions during Adenosine infusion has been shown to be a strong, independent predictor of subsequent coronary events and worse outcome, particularly in association with ischemic defects. However, the prognostic significance of Adenosine-induced ST-segment depressions in patients with normal MPI is not known.

Methods: We performed a retrospective analysis of 3,231 patients undergoing Adenosine MPI. Patients with baseline electrocardiographic (ECG) abnormalities were excluded. Overall, 228 (7%) patients developed ischemic ECG changes (ST-depression ≥1mm) during Adenosine infusion. Of these, 66 (29%) had no perfusion defects on MPI. The incidence of death, nonfatal myocardial infarction (MI) and need for subsequent revascularization was analyzed at a mean follow up of 33±14 months.

Results: Compared to 1,401 patients without ST-depressions during Adenosine and normal MPI, patients with Adenosine-induced ischemic ECG changes were more likely to be women, with more known coronary artery disease, and history of both prior revascularization and MI. Follow up was complete in 85 patients (60%) with ischemic changes during Adenosine. During follow up, there were 3 deaths (all cardiac), and 5 nonfatal MI (12% risk of death and nonfatal MI). Of 13 patients referred for cardiac catheterization, 11 (85%) had significant coronary disease, and 10 underwent surgical or percutaneous revascularization. Of the index stress test, 7 had ischemic ECG changes during Adenosine and normal MPI experienced a cardiac event (death, MI, revascularization) during follow up.

Conclusion: Patients with normal Adenosine myocardial perfusion imaging who develop ischemic ST-segment depressions during Adenosine infusion are at substantially high risk of future cardiac events. Ischemic ECG changes during Adenosine infusion should warrant further evaluation even when perfusion images appear reassuring.

11:45 a.m.

817-4 Prognostic Value of Normal Tc-99m Myoview SPECT Imaging: Preliminary Results From the Myoview Multicenter Registry in 4,728 Patients
Leslie J. Shaw, Robert Hendel, Salvador Borges-Neto, Joy Burnette, Rory Hachamovitch, Elizabeth Krawcynska, Naomi Alazraki, Manuel Cerqueira, Jamshid Maddahi, Atlanta Cardiovascular Research Institute, Atlanta, Georgia, UCLA Medical Center, Los Angeles, California.

Background: Event rates associated with normal perfusion scans, as shown by numerous investigators, are <1% per year of follow-up. This uniformly low event rate is critical when applying nuclear test information to risk stratification. Limited prognostic data are available with Tc-99m myoview SPECT.

Methods: We enrolled a consecutive series of 4,728 patients undergoing stress Tc-99m
Myocardial Perfusion SPECT (MPS) provides incremental prognostic value over exercise treadmill testing (ETT) for hard events (HE) [cardiac death (CO) and non-fatal myocardial infarction (MI)]. However, the prognostic value of significant ST segment depression (STD) in the presence of a normal MPS is unknown.

Methods: We identified 5367 consecutive patients who underwent rest TI-201/exercise SPECT imaging at 5 US hospitals. All patients had a norma}