YOUNG INVESTIGATOR COMPETITION
Friday, September 12, 2008, 4:00 p.m. – 5:30 p.m.

21.01

THE RELATIVE ROLES OF MYOCARDIAL PERFUSION IMAGING AND CORONARY ANGIOGRAPHY IN PREDICTING SURVIVAL IN PATIENTS WITH END-STAGE RENAL DISEASE AWAITING RENAL TRANSPLANTATION

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Background: Patients with end-stage renal disease (ESRD) are at high risk for cardiovascular events. This study examined the prognostic power of stress SPECT myocardial perfusion imaging (MPI) in patients who also underwent coronary angiography.

Methods: A total of 150 patients being evaluated for renal transplantation (RT) and who had stress MPI and coronary angiography within 6 months of the MPI were included in this study. Baseline clinical, laboratory, angiographic and mortality data were collected prospectively. Perfusion defect size on MPI was determined by automatic quantitative analysis. All cause mortality was defined as the outcome measure. Survival time was censored for RT.

Results: The mean age was 53 ± 9 years; 30% were women, 66% were diabetic, and 63% had a history of coronary disease. An abnormal MPI was present in 85% of patients and 30% had left ventricular (LV) ejection fraction (EF) ≤ 40%. The mean perfusion defect size (scar + ischemia) by MPI was 22 ± 16% of LV myocardium. The mean number of diseased vessels by coronary angiography was 1.7 ± 1.2; 45% underwent coronary revascularization (CR). At a mean follow-up of 3.4 ± 1.5 years, 53 deaths occurred (35%). LVEF ≤ 40% (OR = 2.6, 1.2-5.3, p = 0.01), LV dilatation (end-diastolic volume > 90 ml) (OR = 3, 1.3-6.9, p = 0.008), and diabetes mellitus (OR = 2.3, 1.1-4.9, p = 0.0004) were associated with a higher mortality while those who underwent RT were less likely to die (OR = 0.13, 0.05-0.36, p < 0.0001). The total perfusion defect size (26 ± 16% vs. 20 ± 16%) and the ischemic defect size (12 ± 11% vs. 8.5 ± 8.5%) were significantly larger in those who died (p < 0.05). Mean number of diseased vessels by coronary angiography was higher in those who died (2 ± 1.2 vs. 1.5 ± 1.2, p = 0.03), though CR (40% vs. 47%) was not statistically different between survivors and non survivors. In a multivariate model comprising abnormal MPI (low LVEF or abnormal perfusion), number of diseased vessels, age and diabetes mellitus, abnormal MPI was a strong independent predictor of death (adjusted OR = 2.5, 1.1-5.3, p = 0.02). Severity of coronary disease by angiography did not impact survival. Patients with moderate and large perfusion defects had worse survival (χ^2 = 6, p = 0.02).

Conclusion: MPI is a strong predictor of all cause mortality in ESRD patients awaiting RT. The combined perfusion defect size and LVEF independently predicted worse survival and provided more powerful prognostic data than the extent of coronary disease by angiography.

21.02

REPEAT SPECT MYOCARDIAL PERFUSION IMAGING AFTER AN INITIAL NORMAL STUDY IDENTIFIES DIABETIC PATIENTS AT HIGH RISK FOR CARDIAC EVENTS

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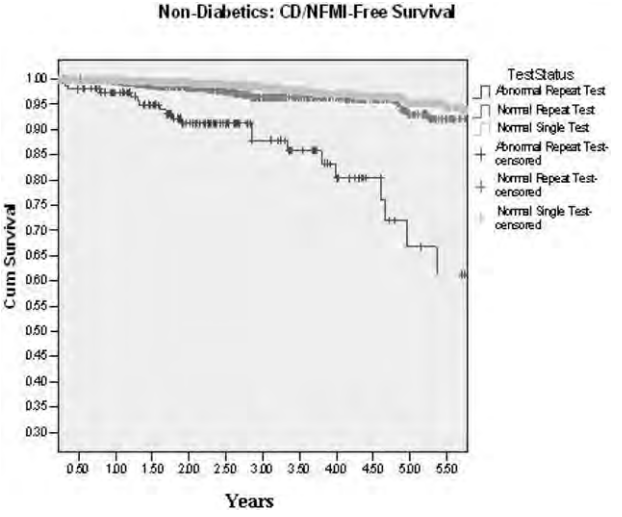
Background: The value of clinically indicated repeat stress myocardial perfusion imaging (MPI) after an initial normal test in high-risk populations, such as diabetic patients, is unknown.

Methods: We evaluated 7,831 patients between 1996 and 2003 who underwent clinically indicated single-photon emission computed tomography (SPECT) MPI: 6,270 non-diabetic (NDM) patients and 1,561 diabetic (DM) patients. Of these, 6,671 patients had single MPI (DM: 1,201, NDM: 5,470), and 1,160 patients underwent repeat MPI after an initial normal study (DM: 360, NDM: 800). Patients were followed for occurrence of cardiac death/non-fatal myocardial infarction (CD/NFMI). Clinical indications for repeat MPI included angina, abnormal ECG, and/or dyspnea. Patients with prior abnormal MPI, known CAD, and revascularization <30 days after abnormal MPI were excluded.

Results: Among DM patients who underwent repeat testing, 288 (80.0%) remained normal and 72 (20.0%) converted to abnormal. Among NDM patients, 650 (81.3%) remained normal, and 150 (18.7%) converted to abnormal. Diabetic and non-diabetic patients with repeat abnormal MPI were significantly more likely to suffer a cardiac event than those with normal MPI.



Conclusions: Clinically indicated repeat MPI is a valuable prognostic tool in diabetic patients with a normal initial study.

21.03

IMPACT OF CREATININE CLEARANCE (CRCL) ON RISK STRATIFICATION OF DIABETICS AND NON-DIABETICS UNDERGOING MYOCARDIAL PERFUSION SPECT (MPS) FOR EVALUATION OF CORONARY ARTERY DISEASE (CAD)

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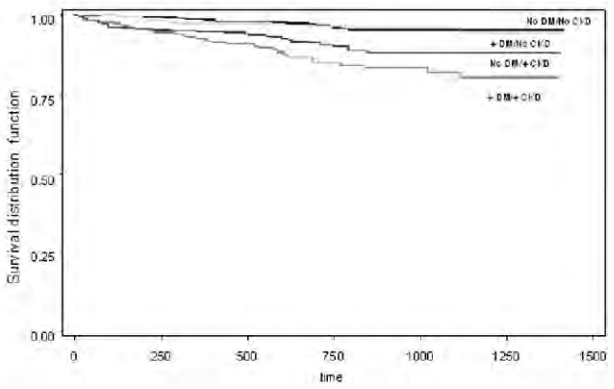
Background: Coronary artery disease (CAD) is the leading cause of death among diabetics, making non-invasive risk stratification desirable. We studied the impact of Creatinine Clearance (CrCl) on risk stratification of diabetic and non-diabetic patients (pts) undergoing myocardial perfusion single-photon emission computed tomography (MPS).

Methods: In this study, 1,747 pts (age 65 ± 10 years) undergoing MPS (32% exercise, 95% gated) were followed for cardiac death (CD) for a mean of 2.15 ± 0.8 years. CrCl was calculated using the modified Modficiation of Diet in Renal Disease (MDRD) equation.

Results: Chronic kidney disease (CKD) alone (CrCl < 60ml/min) was present in 436 pts (25%), DM alone in 332 (19%) pts, and CKD and DM in 297 pts (19%). Annual rate of CD was 1% in pts without DM/CKD, 1.1% in pts with DM alone, but was 2.5% in pts with CKD alone and 3.7% in those with DM and CKD ($p < 0.001$). CKD had a hazard ratio (HR) of 2.00 (95% CI 1.33-3.02) while DM alone had a HR of 1.51 (95% CI 1.02-2.24) for CD in the Cox proportional hazards model after controlling for age, ejection fraction (EF), CAD, hypertension, dyslipidemia, and previous myocardial infarction. High-risk pts (moderate to severely abnormal MPS and ejection fraction [EF] < 40%) with DM and no CKD had a HR 1.67 (1.10-2.56) while pts with both CKD and DM had HR of 2.67(1.73-4.12) for CD. Log-rank test for difference in probability of CD was non-significant for comparison between pts without DM/CKD and those with DM alone ($p=0.91$) but was significant for comparison between pts with no disease and pts with CKD alone ($p < 0.001$) or DM/CKD ($p < 0.001$). (Figure 1.)

Figure 1.



Conclusions: CrCl provides valuable risk stratification for diabetic pts. Cardiac morbidity in diabetics may largely be due to underlying CKD.

21.04

DOES SPECT PERFUSION IMAGING ASSIST IN IDENTIFYING HIGH-RISK ISCHEMIA IN PATIENTS ACHIEVING HIGH EXERCISE WORKLOAD (≥ 10 METS)?

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Background: Cost-effective risk stratification in patients with known or suspected coronary artery disease is essential to reduce adverse cardiac events while limiting expensive, unnecessary testing. High exercise capacity is recognized as a strong predictor of outcomes in patients undergoing stress testing and may identify a population at very low risk of significant ischemia who do not require perfusion imaging. Accordingly, we sought to determine the prevalence of varying degrees of ischemia by exercise single-photon emission computed tomography (SPECT) in patients achieving ≥ 10 metabolic equivalents (METS) regardless of peak heart rate attained. Our comparison was comprised of those reaching ≥ 85% of their maximum predicted heart rate (MAPHR) but low cardiac workload (<10 METS), as those with both low exercise heart rates and workload are already known to be at high risk.

Methods: We prospectively analyzed 1,043 consecutive patients who underwent exercise stress-rest ^{99m}Tc SPECT myocardial perfusion imaging between February 2006 and January 2007 and either achieved ≥ 10 METS of cardiac workload, regardless of their MAPHR (n = 523), or reached ≥ 85% of their MAPHR but < 10 METS (n = 520). Images were analyzed by 3 independent, experienced readers, and the percentage of the left ventricle (%LV) ischemic was calculated using a 17-segment model. We compared the baseline characteristics, exercise parameters, and presence and extent of myocardial ischemia in these 2 cohorts using T-tests and chi-square analysis. We also performed a multivariable logistic regression analysis predicting high risk ischemia (≥1 0% of the LV).

Results: Those attaining ≥ 10 METS were younger and more often male, with lower prevalences of hypertension, diabetes, and obesity (each $p <$ 0.001) than those achieving target HR but < 10 METS. They were less likely to have exercise-related ST-depression ($p = 0.01$) but had no difference in prior myocardial infarction or measured ejection fraction. Those reaching ≥ 10 METS were less likely to have reversible ischemia (5.5% vs. 18.1%, $p < 0.001$) and ≥ 10% LV ischemia (0.57% vs. 5.6%, $p <$ 0.001). Subjects attaining ≥ 10 METS with no exercise ST-depression had only a 0.21% prevalence of ≥ 10% LV ischemia compared with 3.4% for those with lower exercise capacity. Achieving ≥ 10 METS was a strong negative predictor of significant ischemia (odds ratio 0.10 [95% CI 0.03-0.33], $p < 0.001$).

Conclusions: Patients achieving ≥ 10 METS with no exercise ST-depression have an extremely low prevalence of significant ischemia (0.2%), and myocardial perfusion imaging may not be necessary for additional risk stratification. Attaining high cardiac workload during exercise stress is a powerful predictor of a very low probability of significant ischemia regardless of MAPHR. Patients who achieve > 85% of their MAPHR but < 10 METS have > 3-fold and 10-fold higher frequencies of inducible and high-risk ischemia respectively. Thus cardiac workload is a superior predictor of ischemia compared with peak exercise heart rate.

21.05

REPRODUCIBILITY OF A NOVEL FLOW QUANTITATION TECHNIQUE FOR RUBIDIUM-82 PET IMAGING

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Background: Quantitative (Q) measurement of myocardial blood flow (MBF) has the potential to improve assessment of the presence, extent, and severity of coronary artery disease in patients undergoing myocardial perfusion imaging. Calculation of QMBF requires measurements of the blood pool (BP) input function and temporal myocardial uptake. We validated the reproducibility of an automated algorithm to estimate these critical input functions and QMBF through repeated rest scans in Rb-82 PET imaging.

Methods: Eight patients (3 men; mean BMI 22 kg/m^2; 3 with known CAD) were imaged twice at rest on a Biograph-16 PET/CT scanner by injecting 30 ± 5 mCi Rb-82 for each image. The list mode image data was processed automatically for estimating the regional MBF and blood pool input functions by a wavelet-based myocardial boundary detection approach [1]. Flow values were calculated after mathematically fitting the input functions to a simple compartmental model. Reproducibility of the input function calculation was assessed by estimating the average difference (μCi/ml), standard deviation, correlation coefficient and statistical significance between the time activity curves of BP and the myocardial uptake between the two consecutive scans. QMBF (ml/gm/min) values were calculated and compared for 48 total vessel regions as defined by American Society of Nuclear Cardiology Guidelines (16 each LAD, RCA, LCX).

Results: The mean difference in estimation of BP input was -1.32 ± 6.46 μCi/ml ($p = 0.76$, $r = 0.8$) and myocardial uptake was -1.37 ± 5.79 μCi/ml in the LAD ($p = 0.85$, $r = 0.94$), -0.91 ± 7.95 μCi/ml in the RCA ($p =$ 0.84, $r = 0.95$) and -0.005 ± 0.044 μCi/ml in the LCX ($p=0.90$, $r=0.91$) regions. A very high correlation of mean rest QMBF ($r=0.95$, average difference: -0.025 ± 0.095 ml/gm/min, 95% CI: -0.2 - 0.155 ml/gm/min, $p>0.05$) was observed between the two scans (Fig. 1). QMBF difference was equivalent for the 3 vascular territories (average QMBF difference: 6.7% ± 11.6% (LAD), 6.0% ± 10.6% (RCA), 7.7% ± 12.9% (LCX); $p >$ 0.05)).

Conclusions: Quantification of MBF in Rb-82 PET utilizing a wavelet based boundary detection approach and simple compartmental analysis is reproducible within 8%.

[1] Saha K, Hsu BL, Cullom SJ, Helmuth P, Bateman TM, Case JA. An Automated Approach to Quantify Myocardial Blood Flow and Coronary Flow Reserve from Rb-82 PET. JACC 2008.

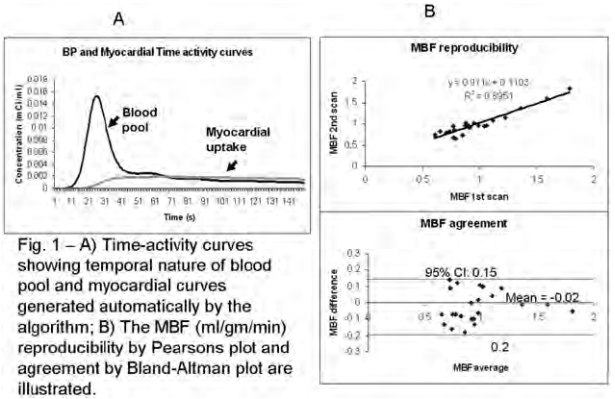

Fig. 1 – A) Time-activity curves showing temporal nature of blood pool and myocardial curves generated automatically by the algorithm; B) The MBF (ml/gm/min) reproducibility by Pearsons plot and agreement by Bland-Altman plot are illustrated.

21.06

STRESS TESTING MODALITIES AND PREDICTION OF ADVERSE CARDIAC EVENTS IN DIABETICS: META-ANALYSIS OF 9,915 PATIENTS

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Background: Diabetes is associated with higher adverse cardiac event rate compared to non-diabetic patients. Identifying diabetic patients at high risk of future cardiac events may help in favorably modifying risk of adverse cardiac events. Multiple imaging techniques are in use for risk stratification. Aim of our analysis was to compare stress echocardiography (echo) and single-photon emission computed tomography (SPECT) myocardial perfusion imaging (SPECT) for prediction of adverse cardiac events.

Methods: PUBMED was searched using various combinations of terms "coronary artery disease", "diabetes", "SPECT", "Imaging", "Echocardiogram", "stress testing", and "Nuclear." Individual study references were hand searched. Studies with less than 50 patients, mean follow-up $<$ 1 year or not reporting incidence of hard events were excluded. Hard events were defined as myocardial infarction or death. Random effects model was used to compare studies due to significant heterogeneity.

Results: Search resulted in 35 studies. Of these, 12 studies met our criteria. A total of 9,915 patients were included (Males 5,344; Females 4,571). Mean age was 64 $\pm$ 3yrs. Mean follow-up was 2.9 $\pm$ 1 years. In all, 4,336 patients underwent SPECT compared to 5,579 in Echo group. A total of 5,690 (57%) patients had an abnormal study (SPECT = 2348; Echo = 3342). A total of 1,845 adverse events (18.6 %) occurred over 3 years: 1,418 (25%) in those with a positive study compared to 427 (10%) in those within the negative study group. Patients with abnormal SPECT had a higher odds ratio of hard events compared to those with an abnormal Echo (OR 6.46, CI 2.72-15.33 vs 2.284, CI 1.63-3.19, respectively). Average annual event rate in SPECT group was (9.6 vs 2.3 ; positive vs negative, respectively) compared to Echo (10.3 vs 7.7).

Conclusion: Diabetics with an abnormal stress test irrespective of testing modality have a 3.5 fold higher adverse cardiac event rate compared to those with normal study. Patients with a positive SPECT study have a 4 fold higher risk of having an adverse event compared to those with a positive Echo. SPECT, as compared to Echo, more effectively identifies diabetic patients at higher risk for adverse cardiac events who may require more aggressive therapy and preventive measures.

21.07

VALIDATION OF A DIGITAL ELECTRONIC STETHOSCOPE IN DIAGNOSING CORONARY BLOOD FLOW ABNORMALITIES VERSUS MYOCARDIAL PERFUSION IMAGING OR CT ANGIOGRAPHY

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Background: Currently available methods for the detection of coronary artery disease (CAD) are compromised by various factors, including high cost and exposure to radioactivity and/or contrast dye. The Cardiac Sonospectrographic Analyzer (CSA; SonoMedica Model 100) represents a potential alternative to existing modalities for diagnosing CAD. The CSA is a digital electronic stethoscope designed to identify microbruits (400-1200 Hz) characteristic of abnormal blood flow in atherosclerotic arteries. The CSA has not been validated prospectively as a screening tool for CAD. We hypothesize that the CSA will provide high predictive values for the detection of abnormal coronary blood flow in patients with atheromatous disease.

Methods: The CSA exam is performed by placing the transducer over 9 positions on the chest and recording heart sounds for 30 seconds at each position. An algorithm synchronized to a simultaneously recorded ECG is used to generate a "flow microbruit score" (FMS). Gender-specific FMS cut points established in prior case series were used to identify abnormal scores. Outpatients referred for the diagnosis of CAD by nuclear myocardial perfusion imaging (MPI) or cardiac CT angiography (CTA) were examined prior to their scheduled tests. The MPI and CT scans were read by faculty radiologists and cardiologists who were blinded to patients' FMS scores. An abnormal scan was defined as one with a high likelihood of flow-limiting disease. An abnormal nuclear scan was defined as a summed stress score of $>$8, and an abnormal CT scan as greater than or equal to 70% stenosis in any major epicardial coronary artery.

Results: One hundred fourteen patients between the ages of 26-85 were studied; results are summarized in Table 1.

Table 1.

	Sensitivity	Specificity	PPV	NPV
Nuclear MPI, n=26				
Abnormal MPI (6)	.85	1	1	.95
Cardiac CTA, n=88				
Abnormal CT (7)	.89	1	1	.99

Conclusion: The CSA is a novel non-invasive technology, and may represent an inexpensive and rapid screening device for detecting abnormal coronary blood flow as occurs in atherosclerotic heart disease. We have found that the CSA has excellent sensitivity, specificity, and predictive values in the outpatient setting using nuclear MPI or cardiac CTA as the gold standard.