

Posters Display III Clinical Outcome and PET

08:30-12:30

7.1

Cold pressure testing 99 Tc MIBI-SPECT detecting abnormal coronary vasoreactivity in asymptomatic population at moderate risk of cardiovascular events. PARADIGMA multicenter study.

N. Nestor Perez Baliño¹, O. Masoli¹, S. Trautwein¹, J. Lynberg¹, C. Rappallo², M. Redruello², D. Rosa², D. Cragolino², A. Meretta², L. Vidal¹. ¹Hospital Argerich, Nuclear Cardiology-Div Cardiology, Buenos Aires, Argentina, ²Inst. Cardiovascular de Buenos Aires, Nuclear Cardiology-Div Cardiology, Buenos Aires, Argentina

Correlation between Cold Pressure Testing (CPT)/ 99 Tc MIBI-SPECT defects and intracoronary acetylcholine (ACH) paradoxical constriction was published by our group. The usefulness of CPT non-invasive diagnosis of dysfunction (ED) was demonstrated by our observation in coincidence with other authors. There is little information on ED incidence on moderate risk asymptomatic (MRA) patients according to ATP III/Framingham index. Objective: This study is aimed at analyzing the incidence and localization of 99 Tc MIBI/ SPECT myocardial perfusion (MP) defects during CPT as indicator of ED on MRA patients. **Methods:** 124 patients (78 female) currently compounding PARADIGMA Study Register were analyzed. PARADIGMA is a prospective multicenter study that will include once completed a total number of 450 MRA patients according to ATP III/Framingham index (< 20% events at 10 years), with normal exercise MP and no cardiovascular disease history. CPT-MP imaging was obtained in all these patients. MP extension score was used in a 17 segment model, reported by two observers on consensus. Mann-Whitney U Test statistical analysis was performed. **Results:** positive CPT 25/113 patients (22,12 %). CPT extension perfusion score positive $5,77 \pm 2,38$ ($p < 0,0001$). CPT was positive in 30,76 % men and 17,56 % women ($p < 0,001$). Localization: anterior wall 43 %, inferior wall 47 %, lateral wall 4,5% and anterior with inferior walls 4,5 %.

Conclusion: These results suggest high incidence of ED on MRA patients, who are also free from exercise -- related ischemia. There were no significant differences in clinical data and defects localization. Further studies will indicate whether this positive CPT population would have higher risk of cardiovascular events during follow-up

Age, Blood Pressure and Cholesterol

pns (*)	AGE	SBP	DBP	CHOLEST.	HDL	LDL	TRIGL.
CPT (+)	55.9 ± 10	130 ± 12	84 ± 5	245 ± 90	48 ± 19	156 ± 49	246 ± 143
CPT (-)	53.5 ± 9	129 ± 15	79 ± 9	228 ± 45	51 ± 12	157 ± 34	160 ± 72

7.2

Effects of percutaneous intramyocardial plasmid gene transfer of vascular endothelial growth factor (phVEGF-A165) on myocardial perfusion measured by N-13 ammonia-PET.

S. Graf¹, A. Aliasghar Khorsand¹, M. Gyongyosi¹, G. Karanikas², H. Eidherr², K. Kletter², G. Porenta³, D. Glogar¹, H. Sochor¹. ¹Medical University of Vienna, Cardiology, Vienna, Austria, ²Medical University of Vienna, Nuclear Medicine, Vienna, Austria, ³Rudolfinerhaus, Vienna, Austria

Aim: Therapeutic angiogenesis is a new therapeutic option for ischemic myocardium without abilities of revascularisation. In a substudy of the Euroinject One randomized double-blind trial, the effects of percutaneous intramyocardial plasmid gene transfer of vascular endothelial growth factor (phVEGF-A165) on myocardial perfusion were investigated.

Methods: Nine patients (2 females, 7 males, age 61 ± 8) with severe stable ischemic heart disease, CCS 3, and no options of conventional coronary revascularization were randomized to receive either 0.5 mg phVEGF-A165 (VEGF; n=5) or placebo (n=4) plasmid in the ischemic myocardial region, using NOGA catheter system. Myocardial perfusion was measured by N-13 ammonia PET at rest and under pharmacologic vasodilation with adenosine.

Results: No differences in coronary flow reserve (CFR) were found between the 2 groups at baseline. After 3 months, CFR improved insignificantly in VEGF group (global CFR from $1,38 \pm 1,01$ to $1,74 \pm 0,78$; $p = n.s.$; regional CFR in the area of VEGF injection from $1,05 \pm 0,38$ to $1,69 \pm 1,09$; $p = n.s.$), and was unchanged in Placebo group (from $1,68 \pm 0,35$ to $1,56 \pm 0,53$; $p = n.s.$; regional CFR from $1,36 \pm 0,27$ to $1,17 \pm 0,43$; $p = n.s.$). The difference between the groups remained insignificant.

CCS classification of angina improved significantly in both groups, but without difference between the groups. No phVEGF-A165-related adverse events were observed while NOGA procedure-related adverse events occurred in 1 patient.

Conclusions: Although, no significant difference between VEGF or placebo treated patients could be demonstrated at 3-month follow-up, a slight increase in CFR could be observed after VEGF therapy. Transient VEGF overexpression seems to be safe.

7.3

Effects of spinal cord stimulation on myocardial perfusion and function measured by N-13 ammonia-PET.

S. Graf¹, A. Aliasghar Khorsand¹, M. Beheshti², C. Poetzi², W. Wadsak², K. Kletter², G. Porenta³, H. Sochor¹, G. Maurer¹, J. Wolfram¹. ¹Medical University of Vienna, Cardiology, Vienna, Austria, ²Medical University of Vienna, Nuclear Medicine, Vienna, Austria, ³Rudolfinerhaus, Vienna, Austria

Background: Spinal cord stimulation (SCS) is a new therapeutic alternative in patients with severe coronary artery disease and no options of revascularization. SCS has been shown to improve anginal symptoms in these patients. However, it is unknown whether myocardial perfusion is altered by SCS.

The aim of our study was to investigate the effect of SCS on myocardial perfusion and left ventricular function.

Methods: Twelve patients (3 females, 9 males; 66 ± 5 years) with severe stable ischemic heart disease, CCS 3, and no options of conventional coronary revascularization were investigated. Myocardial perfusion and left ventricular function were measured by dynamic and gated N-13 ammonia PET at rest and under pharmacologic vasodilation (adenosine) without and with SCS therapy.

Results: No differences in coronary flow reserve (CFR) were found between the 2 investigations ($1,59 \pm 0,54$ without SCS and $1,37 \pm 0,3$ with SCS; $p = n.s.$). EF was unchanged (47 ± 12 % without SCS and 48 ± 12 % with SCS). CCS classification of angina improved significantly under SCS therapy.

Conclusions: Significant improvement of anginal symptoms under SCS therapy may be independent from CFR and EF that remain unaltered by SCS therapy.

7.4

Resting LVEF and transient ischemic dilatation index are predictors of all-cause mortality in patients aged 75 years or older.

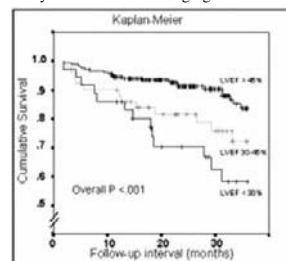
O. Olivier De Winter¹, A. Velghe², N. Van de Veire³, P. De Bondt⁴, M. De Buyzere³, C. Van de Wiele⁴, G. De Backer³, T.C. Gillebert³, R.A. Dierckx⁴, J. De Sutter³. ¹Ghent University Hospital, Nuclear Medicine Division, Ghent, Belgium, ²Ghent University Hospital, Department of Geriatrics, Ghent, Belgium, ³Ghent University Hospital, Cardiology Department, Ghent, Belgium, ⁴Ghent University Hospital, Nuclear Medicine Division, Ghent, Belgium

Aim: Perfusion and functional gated SPECT data have prognostic value in the middle-aged patient population. Our aim was to investigate if these data have incremental value above clinical parameters in patients aged 75 years or older.

Methods: All patients underwent a 2 day stress-rest therosmin gated SPECT study. Resting and post stress left ventricular (LV) ejection fraction (EF) and volumes and transient ischemic dilatation ratio (TID) were calculated using QGS software. Univariate predictors of were investigated using Mann Whitney U testing. Significant univariate predictors were inserted in a stepwise multivariate Cox proportional hazard model to determine independent predictors of mortality.

Results: The population consisted of 294 patients (54% males, median age 78). There were 47 (16%) patients who died during a median follow-up of 25.9 months. A higher resting heart rate and the absence of beta-blocker treatment were independent clinical predictors of mortality (Chi-square= 13.8; $p < 0,001$). Although all LV functional variables (EF and volumes) and the defect extent on stress and rest imaging were univariate predictors of mortality, only a lower resting LVEF (Chi-square gain of 14.9, $p < 0,001$) and a higher TID (Chi-square gain of 6.3, $p = 0,015$) provided independent prognostic value above the clinical model. The figure shows the Kaplan-Meier survival curve in patients with a resting LVEF over 45% and below 30%.

Conclusions: Resting LVEF and TID ratio determined by gated SPECT are important predictors of all-cause mortality and have incremental prognostic value in patients aged 75 years or older referred for myocardial SPECT imaging.



Kaplan-Meier curve

7.5

Post stress end systolic volume and kidney function are independent determinants of NTproBNP levels in elderly patients with coronary artery disease.

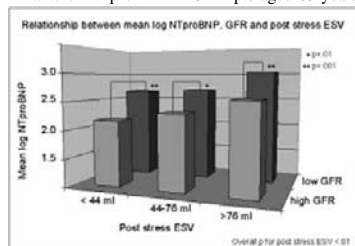
O. Olivier De Winter¹, N. Van de Veire², M. De Buyere², T.C. Gillebert², D. Bernard³, M. Langlois³, R.A. Dierckx⁴, J. De Sutter² ¹Ghent University Hospital, Nuclear Medicine Division, Gent, Belgium, ²Ghent University Hospital, Cardiology Department, Ghent, Belgium, ³AZ Sint-Jan, Department of Biochemistry, Brugge, Belgium, ⁴Ghent University Hospital, Nuclear Medicine Division, Ghent, Belgium

Aim: N-terminal proBNP peptide (NTproBNP) is a valuable tool in the diagnosis of heart failure and has a prognostic value in CAD patients (pts). Parameters derived from gated SPECT and kidney function have however also a strong prognostic value in these pts. Our study aim was to assess whether gated SPECT data and kidney function are independent determinants of NTproBNP in CAD pts above 65 years.

Methods: We studied 131 consecutive pts with stable CAD referred for myocardial perfusion imaging. Left ventricular (LV) volumes were derived from myocardial gated SPECT data. Summed stress, rest and difference scores were calculated using semi-quantitative 4DM SPECT software (Michigan U). Glomerular filtration rate (GFR) was calculated with a validated equation based on serum creatinine level. Univariate clinical and SPECT determinants of NTproBNP were investigated using ANOVA. A linear regression model was used to determine independent predictors of log NTproBNP.

Results: The study population consisted of 131 pts (79 males, mean age 71 ± 6 y). Univariate predictors of a higher NTproBNP were a lower GFR (p<.001), a longer QRS duration (p=.008), higher resting & post-stress end-diastolic and end-systolic (ESV) volumes (all p<.001) and a higher summed stress and rest score (both p<.001). GFR (F change = 44.4; p<.001) and post stress LV ESV (F change = 31.5; p<.001) were the only independent determinants of log NTproBNP in the regression analysis. In the figure mean log NTproBNP values in these pts are shown according to a low versus high GFR (divided on the median) and post stress LVESV (divided in tertiles).

Conclusion: Post stress LV ESV and kidney function (assessed by GFR) are the main independent determinants of NTproBNP in CAD pts aged 65 years or older.



Figure

7.6

The use of logistic regression analysis based on clinical epidemiological data and treadmill test results to select patients to undergo myocardial perfusion scintigraphy.

P.S. Paulo Duarte¹, L.E. Mastrocolla¹, C.R.E. Sampaio¹, J.M. Rossi¹, P.E. Smanio¹, E.V. Lima¹, C.A.R. Oliveira¹, J.C.R. Pereira² ¹Fleury-Centro de Medicina Diagnóstica, Nuclear Medicine, São Paulo, Brazil, ²Health Public School-USP, Epidemiology, São Paulo, Brazil

Background: early detection of coronary atherosclerotic disease (CAD) is important to prevent death and disability. Myocardial perfusion scintigraphy (MPS) has the appropriate diagnostic and prognostic applications for patients who have an intermediate or high likelihood of disease, but it may not be cost-effective and should be performed only when reasonable doubt is left from other less sophisticated approaches. Based on clinical-epidemiological (CE) probability algorithms of CAD, patients classified as low likelihood of disease might either have no testing or simply undergo exercise testing (EXT). If the EXT results negative the patient is simply followed up; if the EXT is positive, the nuclear test is appropriate. Although this information is useful, it has some problems when in clinical practice. The challenges are how to adequately define patients in terms of likelihood of disease and how to integrate the pre-test probability with EXT results. Objective: to create and evaluate a logistic regression equation to classify patients to be referred to MPS based on the analysis of CE and EXT data. Methods: CE and EXT data on 2099 patients who had MPS performed in a nuclear medicine laboratory from 06/2000 to 06/2003 were collected for analysis. None of these patients had previous history of CAD. Each one was classified by utilizing a modified CE score based on the Framingham study database and EXT information derived from Duke Score (DS). The patients with abnormal results on MPS were followed for a mean period of 16 months. Comparing CE and EXT results with information on the presence of cardiac event in the patients' follow-up, a logistic regression equation was calculated to estimate the probability of truly abnormal results on MPS. 1052 patients randomly selected were utilized to create the logistic regression equation and 1047 to test the results. It was utilized the ROC curve to check the sensitivity and the specificity of the equation. Results: the logistic regression equation was $y = -5.19 + 0.17CE - 0.16DS$, the ROC curve area was 0.94 (95% CI: 0.92-0.98) and specificity as high as 82% was achieved keeping the sensitivity high (100%). Conclusion: a model based on logistic regression analysis demonstrated to be accurate in the classification of the patients that should undergo MPS, and has the potential to save financial resources, precluding patients with low probability to have truly abnormal result on MPS to perform this test.

7.7

Cardiac events after five years of a normal perfusion myocardial scintigraphy.

P. Paola Smanio¹, P. Beraldo², F. Rodrigues³, A. Thom³ ¹Instituto Dante Pazzanese, Cardiologia nuclear, São Paulo, Brazil, ²Instituto Dante Pazzanese, Coronary, São Paulo, Brazil, ³Instituto Dante Pazzanese, Nuclear Cardiology, São Paulo, Brazil

Studies have already been published, showing a lower risk of cardiovascular events after one year of a normal myocardial perfusion scintigraphy (MPS) in population with and without known significant coronary artery disease (CAD).

The aim of this study is to evaluate the follow up after five years of a normal MPS in a high risk of CAD patients (p) with and without known CAD.

Methods: Were analyzed 2.500 p that performed MPS on 1998. Were selected 300 p with normal MPS. Patients were divided in two groups: A group: 140 p with known CAD; and B group: 160p without known CAD. All p have at least 3 risk factors for develop CAD (Hypertension, diabetes, tabagism, high cholesterol blood levels, obesity and familiar history of CAD). All studies were performed with sestamibi-Tc-99m by tomographic technique (SPECT). From the total, 120 p had performed exercise and 180 pharmacological stresses with dipyridamole. As hard event were considered cardiac death and myocardial infarction (MI) and as soft cardiac events were considered cardiac bypass surgery (CABG), angioplasty/Stent implantation and cardiac catheterization (CATH) at the 5 year follow up. Were considered as normal MPS when there were no perfusion defects after the stress imaging.

Results: Verify at the Table bellow. There was no significant difference (p=0,10) between the 2 groups in despite of hard events. In both groups there were a small number of hard events in five years (10/300=3%). In considering soft events, were observed at A group: 35/140=25% and at B group: 16/160=10%.

Conclusion: The results may suggest that even after 5 years, patients with a normal MPS have a low prevalence of hard events. In despite of soft events, the prevalence was higher in patients with known CAD.

Cardiac Events

	Death	MI	CABG	ATC/STENT	CATH
A group	3(2%)	3(2%)	2(1,4%)	8(5,7%)	25(17,8%)*
B group	2(1,2%)	2(1,2%)	5(3,1%)	5(3,1%)	6(3,7%)

Death: cardiac death; MI:myocardial infarction; CABG: bypass surgery; ATC/STENT: angioplasty/Stent implantation; CATH: coronary angiography;* p < 0.05

7.8

Myocardial efficiency reserve predicts the deterioration in exercise capacity over time in patients with heart failure.

K. Keiichiro Yoshinaga, H. Ukkonen, I. Burwash, R. DeKemp, W. Dafeo, R. Davies, H. Haddad, T. Ruddy, J. DaSilva, R. Beanlands. University of Ottawa Heart Institute, Cardiac PET Centre, Ottawa, Canada

Backgrounds: Myocardial efficiency (ME) and ME reserve (MER) can be estimated non-invasively using C-11 acetate PET measurement of oxidative metabolism and echocardiographic measurement of stroke volume (SV) at rest and during dobutamine infusion. In patients with heart failure (HF), ME has been shown to be a predictor of survival. However, the potential utility of ME or MER for predicting the functional capacity of HF patients in follow-up has not been defined. We investigated whether ME and MER could provide prognostic information on the exercise (Ex) capacity of HF patients over time. Methods: 25 patients with HF were prospectively studied [age=66±8 yrs, LVEF=31±8%, ischemic (n=18)]. ME was estimated by the Work-Metabolic Index (WMI = SV index (SVI) × HR × systolic BP/ k-mono, where k-mono is the monoexponential fit of the myocardial C-11 acetate PET time-activity curve). MER was derived from the % change of WMI between rest and during dobutamine infusion (10 µg/kg/min). Ex capacity [maximal oxygen uptake (Peak VO2)] was measured at baseline and at 6 months follow-up in all patients. Worsening Ex capacity was defined as ≥ 10% decrease in peak VO2. Results: At the baseline study, dobutamine infusion resulted in an increase in SVI (35±9 to 40±9 ml/m², p<0.001), k-mono (0.047±0.009 to 0.061±0.013/min, p<0.001) and WMI (6.1±1.7×10000 to 7.9±1.8×10000, p<0.001). MER was 32±26%. From baseline to 6-month follow-up, Ex workload and peak VO2 decreased from 4.8±1.4 to 4.3±1.1 METS (p<0.03), and 16.7±4.8 to 15.2±3.8 ml/kg/min (p=0.057), respectively. Among rest and dobutamine parameters, only MER correlated with the change in Ex capacity over time (r=0.56, p<0.005). An MER ≥ 35% predicted a worsening exercise capacity with a sensitivity, specificity, PPV and NPV of 79%, 82%, 85%, and 75%, respectively. Conclusions: Myocardial efficiency reserve correlates with the change in exercise capacity over time in patients with HF. A myocardial efficiency reserve ≥ 35% predicts functional deterioration with good accuracy. The myocardial efficiency reserve may be a useful clinical prognostic parameter in heart failure patients.

7.9

Prognostic value of rubidium-82 perfusion positron emission tomography in patients referred after SPECT imaging.

K. Keiichiro Yoshinaga, B. Chow, R. DeKemp, K. Williams, L. Garrard, A. Szeto, M. Aung, R. Davies, T. Ruddy, R. Beanlands. University of Ottawa Heart Institute, Cardiac PET Centre, Ottawa, Canada

Background: Previous studies have suggested that positron emission tomography (PET) myocardial perfusion imaging has superior accuracy than SPECT for the diagnosis of coronary artery disease. However, its role in clinical practice continues to be evaluated. The purpose of this study was to determine the prognostic value of Rubidium-82 PET for prediction of cardiac events (cardiac death, myocardial infarction, revascularization, and cardiac hospitalization) in patients who were referred for PET imaging after perfusion SPECT imaging.

Methods: We studied 393 consecutive patients who underwent dipyridamole stress/rest Rubidium-82 PET and were followed for 3.2 ± 1.2 years. 92 patients of these had been referred after a Tc-99m perfusion SPECT study. PET imaging was visually assessed using a 17 segment model scored on a 5 point scale (0=normal, 4=absent uptake). Summed stress score (SSS), summed rest score (SRS), and summed difference score (SDS=SSS-SRS) were calculated. SSS and SRS were divided into 4 groups (< 4=normal; 4 to 7=mild, 8 to 11=moderate, and > 11=severely abnormal). SDS ≥ 2 was considered a reversible defect abnormality.

Results: Among the 92 recent SPECT studies, 12 had been reported as normal, 75 had reported attenuation artifacts and 5 cases were abnormal. All 5 abnormal SPECT studies were abnormal on PET and were not included in this outcome analysis. Among the remaining 87 patients with normal or possible attenuation SPECT studies, PET was abnormal in 12 and normal in 75 cases. During the follow-up period for these 87 patients, 13 cardiac events occurred: 1 myocardial infarction, 5 late revascularization (> 3 months) and 7 hospitalizations due to angina. Patients with normal PET scans had a 94.7% (71/75) event-free survival (mean follow-up: 3.2 yrs) (1.65%/year event rate), compared with 25% (3/12) event-free survival in patients with abnormal PET scans (23.4%/year event rate) (chi-square, $p < 0.01$).

Conclusion: Rubidium-82 perfusion PET has prognostic value in patients with coronary artery disease referred after SPECT imaging. In patients in where diagnostic results are uncertain after SPECT imaging, Rubidium-82 PET provides excellent clinical utility.

7.10

Impact of type 2 diabetes on myocardial perfusion and glucose uptake in areas supplied by stenotic and non-stenotic coronary arteries.

H. Hanne Sondergaard¹, M. Bottcher¹, MM. Madsen¹, O. Schmitz², TT. Nielsen¹, HE. Botker¹. ¹Aarhus University Hospital, Skejby, Department of Cardiology, Aarhus N, Denmark, ²Aarhus University, Department of Clinical Pharmacology, Aarhus, Denmark

Background: Type 2 diabetes (T2DM) is recognized as a state of whole-body insulin resistance (IR). Myocardial IR appears to be present in T2DM with coronary artery disease (CAD), but not in T2DM patients without concomitant CAD. However, it is not clear whether myocardial IR is present in areas supplied by a stenotic or a non-stenotic coronary artery.

The aim of the study was to compare basal and insulin stimulated myocardial perfusion and glucose uptake in areas supplied by a stenotic (S) and a non-stenotic (NonS) coronary artery in CAD patients with or without T2DM, and in healthy controls.

Method: We studied 9 patients with T2DM and angiographically verified CAD (61 \pm 8 years), 9 patients without T2DM but with CAD, and 8 matched controls without T2DM or CAD (56 \pm 6 years). Patients had one area supplied by a stenotic artery, at least one area supplied by a non-stenotic artery and preserved left ventricular function. Myocardial perfusion and MGU were measured with PET using ¹³N-ammonia as perfusion tracer and ¹⁸F-fluoro-deoxy-glucose as glucose tracer. Perfusion was measured at rest and during dipyridamole vasodilation with and without hyperinsulinemic euglycemic clamp (1mU/kg/min).

Results: Whole body glucose uptake was similar in T2DM and CAD but increased in controls (4.11 \pm 2.8 and 5.45 \pm 3.0 vs. 6.9 \pm 2.3 mg/kg/min, $P=0.05$). Myocardial glucose uptake was similar in NonS and S areas in both T2DM and CAD (0.42 \pm 0.11, 0.39 \pm 0.11, 0.33 \pm 0.08 and 0.37 \pm 0.09 μ mol/g/min, $P=0.4$). These values did not differ from controls (0.34 \pm 0.08 μ mol/g/min, $P=0.1$). Myocardial perfusion at rest was similar in NonS and S areas in T2DM and CAD (0.9 \pm 0.3, 0.8 \pm 0.2, 0.9 \pm 0.3 and 0.8 \pm 0.1 ml/g/min, $P=0.7$). Dipyridamole increased perfusion similarly in T2DM and CAD, but flow reserve was reduced in S areas in T2DM as well as CAD. Insulin did not alter perfusion at rest or after dipyridamole infusion.

Conclusion: Myocardial insulin resistance is not an inherent feature of T2DM irrespective of the degree of epicardial disease and whole-body IR. CAD is also associated with whole body IR, but IR does not affect the myocardium when contractility is preserved.

7.11

Clinical classification of stable angina pectoris patients is not reliable-not even in high risk patients.

P.F. Poulsen¹, H. Højlund-Carlsen¹, A. Johansen¹, H.W. Christensen², W. Vach³, M. Møldrup¹, T. Haghfelt⁴. ¹Odense University Hospital, Nuclear Medicine, Odense C, Denmark, ²Nordic Institute, Chiropractic and Clinical Biomechanics, Odense, Denmark, ³University of Southern Denmark, Statistics, Odense, Denmark, ⁴Odense University Hospital, Cardiology Dept., Odense, Denmark

According to ACC/AHA guidelines patients with chronic stable angina based on history, clinical judgment and estimation of pretest likelihood of coronary artery disease (CAD) should be referred directly to catheterization and eventually invasive revascularization. However, in patients with a normal myocardial perfusion imaging (MPI) scan, invasive procedures mean a stepping up in risk, especially in elderly and high risk patients.

Aim: To compare clinical classification and pretest probability estimates in these patients with the outcome of MPI and coronary angiography (CA), 50% diameter stenosis indicating significant CAD.

Methods: 476 patients (aged 57.7 ± 9.1 years) referred to CA for known or suspected stable angina estimated their degree of chest pain (0=no pain; 10=worst pain) on a visual analog scale (VAS) before a single physician judged their type (typical angina, atypical angina, non-cardiac or no chest pain) and Canadian Cardiovascular Society (CCS) grade (0-4) of chest pain. Pretest likelihood of CAD was estimated based on type of chest pain, age, and gender. All patients underwent MPI followed by CA in mean two months later. Blinded design was used throughout.

Results: The table displays data from the approximate "upper half" of the patients, i.e., patients with expectedly more severe disease. It appears that 37%-46% of this category of patients had a normal MPI, and that 35%-53% had insignificant CAD. About 25% of patients with a pretest likelihood of CAD >94% had a normal MPI.

Conclusion: In patients referred to CA for known or suspected stable angina, clinical classification and a simple system for the prediction of CAD is unreliable with regard to myocardial perfusion status and the presence of significant angiographic disease.

Table 1

	MPI Normal	MPI Reversible	MPI Mixed	MPI Fixed	CA O VD	CA 1 VD	CA 2 VD	CA 3 VD
VAS score >3(n=254)	46%	25%	17%	12%	53%	17%	13%	17%
Typical angina (n=279)	41%	31%	17%	11%	41%	20%	19%	20%
CCS grade >1 (n=272)	38%	31%	20%	11%	41%	21%	17%	21%
High pretest likelihood (n=224)	37%	34%	19%	10%	35%	19%	22%	24%

Clinical classes vs results of MPI and CA (VD = vessel disease)

7.12

Relationship between symptoms and perfusion status before and after revascularization in patient with stable angina pectoris.

A. Allan Johansen¹, P.F. Højlund-Carlsen², H.W. Christensen³, W. Vach⁴, M. Møldrup², T. Haghfelt⁵. ¹Odense University Hospital, Department of Nuclear Medicine, Odense C, Denmark, ²Odense University Hospital, Nuclear Medicine Dept., Odense, Denmark, ³Nordic Institute, Chiropractic and Clinical Biomechanics, Odense, Denmark, ⁴University of Southern Denmark, Statistics Dept., Odense, Denmark, ⁵Odense University Hospital, Department of Cardiology, Odense C, Denmark

Aim: We wanted to examine the relationship between symptoms and perfusion before and after revascularization in patients with stable angina.

Methods: 380 patients (147 females), aged 58.0 ± 8.8 years, referred to coronary angiography due to known or suspected stable angina were classified as suffering from typical/atypical angina or non-cardiac chest pain/no pain. Myocardial perfusion imaging (MPI) using a dual isotope (exercise/pharmacological 169/211) protocol was performed. The choice of management (revascularization or medicine only) was based on history and angiographic findings since the MPI results were not communicated. Follow-up, including repeat MPI, was completed after 2-years.

Results: 144 (38%) patients were revascularized. Initially, 320 (84%) had typical/atypical angina and 160 (16%) non-cardiac chest pain/no pain. At follow-up, 145 (38%) had typical/atypical angina, while 235 (62%) had non-cardiac chest pain/no pain. However, when separated according to treatment, a significant difference could be demonstrated in revascularized patients only. Sum stress score (SSS) was significantly reduced in revascularized patients, and not significantly changed in non-revascularized patients. The relationship between type of chest pain and perfusion status in revascularized patients is shown in Figure 1. Among patients with initially typical or atypical angina (designated typ), it was only those who had non-cardiac chest pain or no pain at follow-up (designated ncp) who had a significant reduction in SSS. In non-revascularized patients, there were no significant changes.

Conclusion: A relationship between perfusion and angina type was documented in that relief of typical or atypical angina was associated with improvement of perfusion.

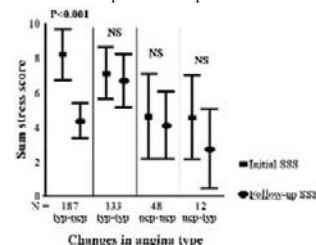


Figure 1

7.13

Metabolic support with glutamine or glutamate was not cardioprotective in a porcine model assessed by MPI.

J. Jens Hedega Kristensen¹, M. Maeng², U.M. Mortensen², JS. Berg², M. Rehling¹, TT. Nielsen.² ¹Skejby University Hospital, Nuclear Medicine, Aarhus., Denmark, ²Dept. of Cardiology, Aarhus, Denmark

Objective: Previous experimental studies indicate that glutamine or glutamate may be cardioprotective by improving oxidative metabolism in myocardial ischemia. We investigated the effect of glutamine or glutamate, given during reperfusion on resulting infarct size, assessed by m99Tc-sestamibi MPI.

Design: A porcine coronary occlusion model was applied. Infusions were initiated 15 min before reperfusion, and supplemented with intracoronary bolus infusions at reperfusion. Primary outcome measures were infarct size (IS) in relation to area at risk (AAR), assessed by myocardial perfusion imaging with m99Tc-sestamibi (MPI) and a standard tissue staining procedure for comparison.

Results: Determined by histochemistry the IS/AAR (mean ± SD) were: Control group: 0,64 ± 0,19 (n=9), Glutamine group: 0,87 ± 0,07 (p< 0,05 vs. control group) (n=8), Glutamate group: 0,72 ± 0,11(n=9). Corresponding values determined by MPI were: Control: 0,87 ± 0,3, Glutamine group: 0,97 ± 0,04, and for glutamate group: 0,85 ± 0,13. Glutamine increased systemic vascular resistance, while glutamate preserved cardiac output during infusion.

Conclusion: Substrate supplementation with the anaplerotic precursors glutamine and glutamate are ineffective as adjunctive therapy for severe myocardial ischemia. Beneficial effects documented in less complex experimental systems could not be transferred to a more pathophysiological relevant model. In vivo MPI is almost as precise in assessing the IS/AAR compared to ex vivo histochemistry, also reflecting smaller differences in IS.

7.14

Relation of stress myocardial perfusion defects and left ventricular function parameters as assessed by gated single photon emission tomography using 99mTc-sestamibi.

K. Khaled ElSaban¹, T. El-Kady², M. El-Gabaly², A. Yehia², M. El-Sayed.³ ¹Faculty of Medicine, Cairo University, Nuclear Medicine, Cairo, Egypt, ²National Heart Institute, Nuclear Cardiology, Cairo, Egypt, ³Assuit University, Nuclear Medicine, Assuit, Egypt

Background: Infarct size (and severity) and LVEF (and volumes) derived from a gated SPECT study correlate closely. However, till our knowledge there is no detailed information about the recent summed score and left ventricular function and to which extent it affects EF.

Aim of the Study: to identify the correlation between the size of myocardial perfusion defect during exercise and both ejection fraction and LV wall motion abnormalities obtained by gated SPECT (gSPECT) and to determine threshold level of SSS contributing to reduction of EF below 40%.

Patients and Methods: 30 patients with known coronary artery disease had been subjected to exercise 99mTc-MIBI gSPECT and resting echocardiography. Myocardial perfusion and resting echocardiography had been divided into 17 segments with scoring of myocardial perfusion using 0-4 score and summing the score at stress (summed stress score SSS), rest (summed rest score SRS) and getting the difference (summed difference score SDS). Wall motion assessment had been done in both resting echocardiography and gSPECT using 1-4 score.

Results: SSS had been found to had modest inverse correlation with EF detected angiographically (r=-0.05981), echocardiographically (r=-0.5504), and by gSPECT at rest (r=-0.5242) and stress (r=-0.6398). In addition, patients with EF >40% (7 patients) had higher SSS than patients with EF<40%. Accordingly, receiver operating curve (ROC) could separate these two groups by SSS > 10. Concerning wall motion abnormality(WMA), perfusion status showed similar affection of WMA by both echo and gSPECT, with modest correlation between SSS and wall motion score measured by either techniques and higher tendency for gSPECT.

Conclusion: Using gSPECT is very informative in patients with CAD. SSS is correlated with EF with the ability of detection of patients with lower EF using SSS >10.

7.15

Motion detection and correction for dynamic cardiac PET water studies.

A. Alexandru Naum, M.S. Laaksonen, H. Tuunanen, V. Oikonen, J. Kempainen, M.J. Järvisalo, P. Nuutila, J. Knuuti. Turku University, Turku PET Centre, Turku, Finland

Background: Patient motion during dynamic PET studies is a well documented source of errors. Frame to frame misalignment will modify the measured time activity curve from a selected region of interest (ROI) which can affect results.

We have developed a motion detection algorithm and examined two registration methods for dynamic cardiac PET water studies, based on alignment of each PET frame with a reference image.

Methods: Normal volunteers underwent a 150-water PET flow study at rest, during adenosine infusion and bicycle exercise in the same session. Before PET acquisition two external radioactive skin markers (22Na) were placed on the back of the patient at the level of thoracic vertebra T7. Space coordinates on X, Y, Z-axis inside the FOV has been determined, and the corresponding (pixels) distance from the origin of FOV was recorded in each frame.

The highest number of frames having identical markers spatial coordinates reported to origin of FOV during the study were defined as non moved.

A reference image obtained by summing all non-moved frames was used for further alignment. Registration was performed manually and automatically by applying a least squares registration algorithm. Values of myocardial blood flow were calculated using a single tissue compartment model.

Results: In original datasets at rest motion was detected in 4 ± 2 frames, out of 20 analyzed. The corresponding values during adenosine and exercise were 9 ± 3 and 16 ± 2.

Compared to original datasets in manually corrected data, motions was encountered at rest in 2 ± 1, during adenosine, 3 ± 4, and exercise 5 ± 4 frames.

Least squares corrected motion studies presented motion at rest in 1 ± 1 frames, during adenosine and bicycle exercise 2 ± 3 and 1 ± 2.

MBF quantitated values in non corrected datasets were at rest 0.77 ± 0.18 ml/g/min, during adenosine and exercise 2.83 ± 1.17 ml/g/min respectively 1.38 ± 0.39 ml/g/min.

Values after manual and least squares motion correction were at rest 0.74 ± 0.13 ml/g/min, p = 0.74, ns and 0.82 ± 0.4 ml/g/min, p = 0.62 ns, during adenosine 4.03 ± 3.01 ml/g/min, p = 0.23, ns and 4.05 ± 2.93 ml/g/min, p = 0.24, ns.

MBF measured values in corrected studies during dynamic exercise were 1.9 ± 0.33 ml/g/min, p = 0.003 (manually corrected) and 2 ± 0.55 ml/g/min, p = 0.019 (least squares corrected).

Conclusions: The proposed frames realignment methods seems to be feasible in our study, reducing the number of moved frames and provided higher values of myocardial blood flow, during adenosine and dynamic exercise, compared with those without motion correction.

7.16

Correlation between N-Terminal pro-brain natriuretic peptide and myocardial perfusion defects in patients with stable coronary artery disease and normal ejection fraction.

G. Gerald Vanzetto¹, P. Jacon¹, D. Fagret², J. Machecourt.¹ ¹Chu de Grenoble, Cardiologie, Grenoble, France, ²University Hospital, Nuclear Medicine, Grenoble, France

BACKGROUND: The prognostic value of NT-pro-brain natriuretic peptide (NT-proBNP) has been demonstrated in patients with acute coronary syndromes but not in patients with stable coronary artery disease (SCAD). We aimed to determine the relationship between NT-proBNP values and the extent of myocardial perfusion defects on exercise (EST) Tl201 SPECT in SCAD pts with normal ejection fraction (EF > 45%).

METHODS: 88 patients (79 men, mean age 61+8 years) with documented CAD and without history or symptoms of congestive heart failure were included. 53 patients (60%) had a history of previous myocardial infarction > 3 months. Mean EF was 62+11%. NT-proBNP was measured at baseline, peak-EST, and 3 hours after EST (Post-EST).

RESULTS: SPECT was normal in 33 patients (37%, group 1) and abnormal in 55 (63%, group 2-fixed defects n=33, reversible defects n=49). EST data were similar in both groups. We observed a significant but weak correlation between Post-EST NT-proBNP values and the extent of perfusion abnormalities (r=0.49, p=0.001). However, Group 2 patients had higher baseline, peak-EST and post-EST NT-proBNP values than group 1 (Table below). NT-proBNP baseline vs. post-EST variations were also higher in group 2. Post-EST NT-proBNP was predictive of perfusion abnormalities and of moderate-to-severe ischemia (areas under the ROC curves = 0.71 and 0.61 respectively). A post-EST NT-proBNP value < 190 pmol/ml ruled-out moderate-to-severe myocardial ischemia with a negative predictive value of 85%. The accuracy of combined EST and post-stress NT-proBNP was 74% for identifying the presence or absence of significant ischemia.

CONCLUSION: A single post-EST NT-proBNP measure accurately predicts the presence or absence of significant myocardial ischemia in SCAD and can be useful for selecting patients requiring perfusion imaging as second line diagnostic or prognostic tool.

NTBNP values

	Group 1	Group 2
Baseline	107 (52-172)	183 (100-274)*
Peak-Est	119(56-182)	201(110-311)*
Post-EST	122(59-195)	213(108-326)*
Baseline-Post EST	+16 (6-25)	+23 (7-66)*

Value are medians (interquartile range). *p < 0.05 versus Group 1

7.17

The effects of mid-term cardiac resynchronisation therapy on myocardial perfusion at rest and after vasodilation and on myocardial oxygen consumption in heart failure patients.

O. Oliver Lindner¹, J. Vogt², A. Kammeier¹, E. Fricke¹, P. Wielepp¹, D. Baller², B. Lamp², J. Holzinger², D. Horstkotte², W. Burchert² ¹Heart and Diabetescenter NRW, Nuclear Medicine, Bad Oeynhausen, Germany, ²Heart and Diabetescenter NRW, Department of Cardiology, Bad Oeynhausen, Germany

Cardiac resynchronisation therapy (CRT) has shown to improve hemodynamics and clinical symptoms in heart failure patients with broad QRS complex and left bundle branch block (LBBB) morphology. The present study evaluated the effects of mid-term CRT on myocardial blood flow (MBF) at rest, after dipyridamole induced vasodilation, and on myocardial oxygen consumption (MVO2) at rest.

Methods: 16 NYHA III patients (age 65±5 y) with idiopathic dilated cardiomyopathy (ejection fraction 22.6±7.6%) and LBBB (QRS width 187.2±17.5 ms) were studied prior to and after 15 weeks of continuous CRT. The pacemaker was adjusted to its optimal AV-delay and to its optimal pacing site. All patients had a positive acute response (pulse pressure increase > 10%) to a biventricular pacemaker system in an electrophysiologic pretest. Resting MVO2 and MBF of the global myocardium and of the anterior, lateral, inferior, and septal wall were determined from an 11C-acetate PET study and vasodilator MBF after dipyridamole infusion from a 13N-ammonia study.

Results: global MBF at rest, after vasodilation, MBF reserve, and resting MVO2 were found to be below the normal limit at baseline did not change by mid-term CRT, whereas the rate pressure product (RPP) normalized MVO2 decreased (P=0.018). At baseline, the regional analysis revealed significantly higher values of all parameters in the lateral wall than in the other myocardial walls. Under CRT, the regional differences of the resting parameters equalized. All parameters showed a significantly smaller coefficient of variation among the myocardial walls. The hemodynamic data revealed a higher systolic blood pressure (P=0.009). Diastolic blood pressure, heart rate and the RPP remained unchanged.

Conclusion: effects of mid-term CRT on MBF at rest, after pharmacological vasodilation and on MVO2 occur on a regional level. The intraventricular resynchronization is associated with a smaller regional variability of MBF and MVO2 between the myocardial walls. Considering MVO2 and the RPP, there is evidence of an improved ventricular efficiency. Substantial alterations of global MBF at rest, MBF after vasodilation, or MVO2 by CRT are not detectable. This indicates no substantial improvement of the underlying cardiomyopathy within the observation period.

7.18

Integration of function and morphology in cardiac PET/CT: a feasibility study in patients with chronic and ischemic heart disease.

S.G. Stephan Nekolla¹, M. Souvatzoglou¹, J. Hausleiter², N. Henke¹, K. Kruschke¹, F. Bengel¹, M. Schwaiger¹ ¹Technische Universität München, Nuklearmedizinische Klinik, München, Germany, ²Deutsches Herzzentrum Bayern, Munich, Germany

Aim: The key strength of PET is high physiological contrast; however, spatial resolution is only modest. With the success of PET/CT imaging devices in oncology (especially with high quality 16 detector CT systems integrated), this offers excellent means towards an "one-stop-shop" in cardiac imaging. For this purpose, we implemented an integrated approach from acquisition protocols to analysis modules and evaluated their feasibility in viability and ischemia imaging.

Methods: Using a combined PET/CT tomograph (Siemens Biograph 16, LSO detectors), a study population of 10 patients (62±12y, 8 m) with severe 3 vessel disease of the left ventricle (LV) (group V) and 10 patients (59±14y, 9 m) with previous myocardial infarction (group I) was examined. The imaging protocol consisted of an initial low dose CT for attenuation correction and list mode PET imaging after the injection of 300-450 MBq N-13 ammonia for 10 min. In group V, this was followed by 30 min list mode F-18 FDG imaging (300 MBq); in group I the NH3 protocol was repeated under adenosine stress. ECG traces were recorded throughout the measurements. All PET imaging was done in 3D mode and images were reconstructed using an OSEM algorithm. Finally, CT calcium scoring (group I only) and CT angiography (CTA) was performed using an iodine based contrast agent after identifying the optimal injection delay with a test bolus. Regional uptake of NH3 and FDG (group V) as well as regional parameters (myocardial blood flow, flow reserve (only group I), metabolic rate of glucose utilization) were quantified. From the CT data, regional calcifications, wall motion and thickness were delineated. In addition, the coronary tree was visualized.

Results: The protocols took an average of 60 min (group I) and 90 min (group V) to acquire. List mode histogramming and reconstruction required 30-40 min and was followed by 30 min of image analysis. Consequent patient monitoring was found to be mandatory to limit motion resulting in misalignment of emission and morphological information. Although the heart rate in group V was significantly higher and ejection fraction reduced (75±12BPM vs. 55±9BPM and 32±6% vs. 44±12%), wall thickness and wall motion was assessable by CTA in all cases.

Conclusions: Characterization of myocardial tissue based on functional and morphological means is realized within one imaging examination. However, the high complexity of data acquisition, reconstruction and analysis warrants its validation in a larger patient population also taking cost effectiveness and radiation exposure into account.

7.19

Role of myocardial perfusion imaging in evaluation of patients with non transmural myocardial infarction.

P.S. Palaniswamy Shanmuga Sundaram¹, S. Padma¹, K.K. Haridas², S. Kumar¹, M. Zachariah¹ ¹Amrita Institute of medical sciences, Nuclear Medicine, Cochin, India, ²Amrita Institute of Medical Sciences, Adult Cardiology, Cochin, India

Non Transmural Myocardial Infarction (NTMI), also known as Non Q wave Myocardial Infarction (NQMI) was previously dealt as "mild" coronary events due to modest cardiac enzyme level elevations. Substantial evidence now calls for modifying this approach because if diagnosed early & intervened, results in a favorable long-term prognosis. Risk stratification of NTMI pts with Myocardial Perfusion Imaging (MPI) is essential to avoid late complications like recurrent angina, Transmural Myocardial Infarction (TMI) & sudden death. We hypothesized that NTMI might have more residual ischaemia or hibernating myocardium than TMI.

METHOD: 120 pts (M : F = 88 : 32, age range 47 ± 9 yrs) proven / suspected to have MI undergoing MPI for risk stratification between Jan-02 to Sep-02 were analyzed. Pts with previous revascularisation, normal MPI findings were excluded. Pts underwent same day 99mTc SestaMIBI rest-stress gated SPECT. All pts had resting 12 lead ECG & pts with pathological Q waves (width > 0.04 sec & depth > 1/4 R wave) in 2 consecutive ECG leads were classified as TMI. Presence of myocardial scar in at least 2 adjacent segments in MPI without Q wave on ECG was considered to be NTMI. A perfusion defect was defined as < 50% MIBI uptake & a reversible perfusion defect was defined as improvement in tracer uptake from stress to rest images at least by 10% or more. Hibernation was termed when a segment with near normal uptake showing good wall thickening but significant hypokinesia on gated study. ECG analysis was blinded to SPECT study.

RESULT: Results were interpreted visually & with a 20-segment myocardial model. 78 (65%) pts had TMI & 42 (35%) had NTMI. Images were evaluated for presence of stress induced LV dilatation, reversible perfusion defects & wall thickening/motion in gated images. NTMI category pts had a higher incidence of reversible ischemia, hibernation (26/42pts-62%) than in TMI (23/78 pts-30%). Mean segments of viable myocardium (ischaemia + hibernation) in NTMI were significantly more than those in TMI (5.1-3.7 Vs 3.0-2.9 p< 0.05). In NTMI pts of our series, LAD territory segments were more frequently involved than others (5/26-58%).

CONCLUSION: Extent & incidence of reversible ischemia & myocardial hibernation is significantly more with NTMI than TMI. So it is important to risk stratify NTMI pts with myocardial perfusion SPECT enabling aggressive approach to salvage myocardium at risk.

7.20

Clinical predictors and prognostic value of stress induced abnormal TI-201 myocardial perfusion SPECT in asymptomatic patients with diabetes mellitus.

S. Shay Livschitz¹, T. Zornitzi¹, S. Vered², M. Oettinger¹, R. Levy¹, A. Caspi¹, D. Faraggi², H. Knobler³ ¹Kaplan Medical Center, Heart Institute, Rehovot, Israel, ²Haifa University, Haifa, Israel, ³Kaplan Medical Center, Metabolic Diseases Unit, Rehovot, Israel

Background: Coronary artery disease (CAD) is the leading cause of morbidity and mortality in patients with diabetes mellitus (DM). Early identification of high-risk subgroups followed by appropriate therapy may improve survival. The aims of this study were to identify clinical predictors of abnormal myocardial perfusion imaging (AMPI) and to evaluate the prognostic value of AMPI in asymptomatic DM pts.

Methods: Between January 1999 and February 2003, 1587 DM pts underwent a stress TI-201 SPECT. Of these, 302 pts fulfilled the following inclusion criteria: asymptomatic, a minimum of 1 year follow up and available clinical data including DM duration, treatment, complications, albuminuria and blood levels of: creatinine, hemoglobin A1C, HDL (HDL-C) and LDL cholesterol, triglycerids. Cardiac events (CE) were classified as hard (HE=cardiac death, myocardial infarction) and soft (SE=unstable angina, coronary revascularization).

Results: An AMPI was present in 62.9% of the pts with either fixed (23.2%) or reversible (39.7%) TI-201 defect patterns. Pts with AMPI compared with pts with normal myocardial perfusion were more often males (79% vs 41%, p< 0.0001), had higher prevalence of hyperlipidemia (59% vs 41%, p = 0.002), peripheral vascular disease (PVD) (51% vs 36%, p = 0.01), an abnormal resting ECG (59% vs 19%, p< 0.0001), smoking (51% vs 36%, p = 0.0004), a previous history of CAD(HX)(65% vs 13%, p< 0.0001) and a lower HDL-C (41±11 vs 46±13 mg/dl, p = 0.001). The best predictive model of an AMPI included male gender, HX, smoking, PVD and abnormal resting ECG. Within the follow-up period (861±384 days) 48 pts had cardiac events (HE=13, SE=35), 41 of them (83.5%) had an AMPI (chi-square= 12.4, p< 0.0001). The best predictive model of total CE included PVD, low creatinine clearance and AMPI. An AMPI had a significant incremental predictive value over the clinical and laboratory data (chi-square= 8, p = 0.005).

Conclusions: Abnormal myocardial perfusion is frequently present in asymptomatic DM pts. Male gender, hyperlipidemia, a previous history of CAD, smoking, PVD, abnormal resting ECG and a low HDL-C blood level characterize a group of pts having an AMPI. Asymptomatic DM pts characterized by PVD, low creatinine clearance and AMPI are a high-risk group for cardiac events.

7.21

Characteristics of stress induced ischemia in symptomatic versus asymptomatic population without known coronary artery disease: correlation with age, gender and functional capacity.

I. Mats¹, A. Solodky¹, T. Ben-Gal¹, A. Battler¹, N. Nili Zafrir.² ¹Rabin Medical Center, Cardiology Department, Petah Tikva, Israel, ²Rabin Medical Center, Beilinson Campus, Petah Tikva, Israel

According to ACC/AHA guidelines asymptomatic patients with relatively low prevalence of CAD. Myocardial Perfusion Imaging (MPI) is currently not recommended, as its prognostic yield is unclear. The aim of this study was to compare between symptomatic versus asymptomatic patients without known CAD referred for stress MPI in terms of prevalence of ischemia, gender, functional capacity and risk factors.

Methods: During 2002 to 11.03 we consecutively identified 1630 patients without known CAD or any cardiac abnormality, who were referred for MPI. Of whom, 1309 (80%) pts (symptomatic) referral reason was angina or angina equivalent symptoms. The remainder 321 (20%) pts (asymptomatic) the referral reason was positive or unequivocal exercise test or for exclusion of CAD. Comparisons between the 2 groups were performed.

Results: see in the table

Conclusions: The asymptomatic population is younger, male, and has a better exercise tolerance. In spite of this, the prevalence of stress-induced ischemia in asymptomatic patients referred for MPI was similar to symptomatic patients suspected of CAD. However, the severity of ischemia was more significant in the symptomatic patients.

Variable	Symptomatic, n=1309 (%)	Asymptomatic, n=321(%)	p value
Age	62.4±12.8	57.7±12.3	<0.01
Gender (men)	607(46)	208(65)	<0.01
Diabetes Mellitus	270(21)	50(16)	0.01
Hypertension	651(50)	140(44)	0.05
Hyperlipidemia	484(37)	113(36)	NS
Family history	125(9)	31(10)	NS
Smoker	192(15)	37(12)	NS
MPHR(%)	92.6±9.3	94±7.4	<0.01
METS	9.4±2.8	10.7±2.9	<0.01
St depression	239(18)	122(38)	<0.01
TID	119(9)	28(9)	NS
Lung uptake	150(11)	35(11)	NS
Ischemia	325(25)	69(21)	NS
Degree Ischemia	1.53±0.66	1.39±0.62	<0.01
LVEF	58.6±11.1	58.8±7.3	NS

7.22

Correlation between clinical-angiographic and scintigraphic markers in prediction of perfusion and kinetic improvement after mechanical revascularization in acute myocardial infarction.

E. Elisabetta Varani¹, M. Balducci¹, S. Severi², A.L. Patroncini³, G. Vecchi¹, C. Gatti¹, C. Corbelli², R. Casanova³, A. Maresta.¹ ¹S. Maria delle Croci, Cardiology, Ravenna, Italy, ²O.C. per gli Infermi, Nuclear Medicine, Faenza, Italy, ³O.C. per gli Infermi, Cardiology, Faenza, Italy

Purpose of the study is to evaluate which of the clinical-angiographic parameters of acute ischemic extension and efficacy of reperfusion in AMI treated with primary PCI are predictive of infarct size and one month improvement of left ventricular function. To assess this issue we evaluated 35 patients, 32 males, mean age 61±11 years with two rest sestamibi gated SPECT, the first 4 to 6 days and the second 30 to 40 days after primary PCI.

We considered the following parameters: AMI location, number of ECG leads with ST elevation (N° ST), the sum in mm of ST elevation (S mm ST), % ST resolution in the ECG up to 60 minutes after vessel reopening (D% ST), total ischemia duration (symptom onset-balloon time; TI), peak CK MB elevation (MB max) and its timing, pre and post-PCI TIMI flow in IRA, corrected TIMI frame count (cTFC), myocardial perfusion grade (MPG), initial and late infarct size (% of black out on total pixel count, %BO), initial and late EF, initial and late segmental kinetic defects.

Results: N° ST, S mm ST and MB max among initial ischemic extension parameters have significant linear correlation one with another and with initial perfusion defect. TI £ 240 min is related to a lower cTFC, a better late EF and smaller infarct size. D% ST ³ 70% is present in 74% of patients and is associated with a smaller late perfusion defect. MPG = 3, present in 77% of patients is significantly correlated with a better late EF. cTFC has a statistically significant linear correlation with late EF. A late EF ³ 50%, present in 54% of patients, is associated with the following parameters: S mm ST (12±6 vs 19±9 mm, p=.028), D% ST (89±17 vs 67±22%, p=.002), TI (151±80 vs 273±176 min, p=.010), MBmax (183±156 vs 317±177 ng/ml, p=.023), initial EF (50±5 vs 40±11%, p=.001), initial (15±10 vs 30±13%, p<.001) and late BO (12.5±10 vs 24±12%, p=.006). An improvement in EF between the first and the second SPECT was seen in 21/35 pts (60%). These pts showed a shorter TI (165 ± 82 vs 271 ± 193, p = .003) and a lower cTFC (21 ± 6 vs 31 ± 14, p = .02). In 14 patients (40%) we observed a reduction of BO associated with a faster CK-MB peak and a bigger infarct size.

Conclusion: improvement of perfusion parameters and left ventricular function is frequent one month after primary PCI in AMI. A total ischemia duration £ 240 min, cTFC £ 21 and MPG = 3 are the best indicators of late EF and improvement of EF.

7.23

Assessment of acute myocardial infarction evolution in patients undergoing primary angioplasty or thrombolytic therapy: a gated-SPECT longitudinal evaluation study.

C. Corrado Cittanti¹, M. Valgimigli², M. Giganti¹, P. Malagutti², G. Percoco², E. Bagatini¹, S. Panareo¹, N. Avigni², R. Ferrari², L. Feggi.¹ ¹Nuclear Medicine Section, University of Ferrara, Ferrara, Italy, ²Cardiology Section, University of Ferrara, Ferrara, Italy

Aim: it's generally recognized a lack of informations concerning the natural history of hypoperfused myocardial territories after an acute myocardial infarction (AMI) treated with percutaneous or pharmacological revascularization. The aim of this study was to assess the evolution of both perfusion defect and left ventricular function simultaneously, from the acute to the stable phase of AMI using rest myocardial gated-SPECT imaging (GS).

Methods: thirtyfive patients (29M/6F-mean age 62±13yr) without history and/or ECG evidence of previous myocardial necrosis underwent successful primary angioplasty (28) or systemic thrombolysis (7) for AMI. All subjects were studied with rest 99mTc-sestamibi GS (740MBq) after 48-72 hours, 2 and 6 months from the acute event. Summed rest score (SRS), end diastolic volume (EDV), end systolic volume (ESV) and left ventricular ejection fraction (LVEF) were obtained for all scintigraphic studies.

Results: from 48-72 hours to 2 months studies an increase in LVEF values (48.6±14.6 vs 54.8±12.7; p<0.01) and a reduction in both SRS (15.8±8.3 vs 7.8±6.8; p<0.001) and ESV (70.1±43.9 vs 62.1±44.3; p<0.05) data were observed. Moreover no significant statistical differences were noticed from early images to 2 months studies in EDV estimates and between 2 and 6 months studies for all the considered parameters. Finally the correlation between the early assessed SRS and its differential values obtained as SRS at 2 months less SRS at 48-72 hours showed a r=0.58 with a p=ns; the same analysis on LVEF values demonstrated similar findings (r=0.52 with p=ns).

Conclusion: the first interesting data emerging from this study is the significant improvement in terms of ESV, LVEF and SRS values noticed between early post-revascularization studies and 2 months scintigraphy. This aspect may be related to a variable quota of stunned myocardium with an associated impairment of microvascular environment and, likely, of sestamibi driving potentials in the post-acute phase of the ischaemic event. Therefore on the basis of early GS data alone the presence of this unpredictable quota may lead to a variable overestimation of both scar area extension and left ventricular function impairment probably limiting the prognostic role of a rest myocardial scintigraphy if performed a little later an acute coronary syndrome. Moreover the resolution of these phenomenons seems to occur in the majority of cases during the first 8 weeks from the AMI. Larger prospective trials are mandatory to confirm these preliminary findings and to assess their potential impact in clinical practice.

7.24

Flow-mediated brachial artery vasodilation rules out coronary artery disease in patients with peripheral artery disease.

P. Pasquale Perrone Filardi¹, A. Cuocolo², G. Storto², G. Brevetti¹, S. Dellegrottaglie¹, L. Corrado¹, M. Cafiero¹, M. Polimeno¹, A. Zarilli¹, M. Chiariello.¹ ¹Federico II¹ University, Cardiology, Naples, Italy, ²Federico II² University, Nuclear Medicine, Naples, Italy

Peripheral artery disease (PAD) is often associated with coronary artery disease (CAD) and such association substantially worsens prognosis. Thus, ruling out CAD is very relevant in patients with PAD.

Aim: To evaluate whether assessment of brachial artery flow-mediated dilation (FMD) by ultrasound imaging predicts absence of significant CAD in patients with documented PAD.

Methods. We studied 44 (age 62±10) consecutive PAD patients (ankle-to-brachial index <0.90; mean 0.7±0.1) asymptomatic for CAD with FMD and dipyridamole (0.74 mg/kg/min) 99mTc-MIBI SPECT within one week while off drugs. SPECT myocardial images were used to measure regional myocardial uptake using a 17 segment-model.

Results. In PAD patients FMD was significantly reduced compared to 18 age-matched controls (6.8±2.1% vs 11.8±3.1%, p=0.0001). Quantitative SPECT was abnormal (either reversible or fixed defect) in 17 (39%) patients. In patients with abnormal SPECT, FMD was significantly reduced compared to patients with normal SPECT (6.0±2.3% vs 7.3±1.8%, p=0.04). A multivariate analysis including cardiovascular risk factors, ankle-to-brachial index and FMD showed that only the latter was significantly associated with abnormal SPECT (OR=0.63, 95%; CI 0.43-0.3; p=0.02). ROC analysis examining the ability of FMD to predict CAD yielded an area under the curve of 0.74 (p=0.009). An FMD value ≥ 6% yielded a 92% negative predictive accuracy to rule out an abnormal SPECT, with 79% sensitivity, 73% specificity and 58% positive predictive accuracy.

Conclusions. FMD is highly predictive of normal myocardial SPECT in asymptomatic PAD patients. Thus, FMD may represent a useful screening test for CAD in PAD patients.

7.25

Long-term evolution of myocardial perfusion pattern at 99mTc-MIBI SPECT in stable CAD patients maintained on medical therapy.

C. Claudio Marcassa¹, R. Campini², P. Calza², P. Giannuzzi¹, S. Maugeri Fnd IRCCS, Cardiology, Veruno, Italy, ²S. Maugeri Fnd IRCCS, Nuclear Medicine, Veruno, Italy

Background. Few data exist about the evolution of the myocardial perfusion pattern over time in pts with stable ischemic heart disease (IHD).

Aim. Aim of the study was to evaluate changes of stress-rest myocardial perfusion in stable pts with stable IHD in medical treatment.

Methods. 174 consecutive pts (age 60+9, 68% males) with known or suspected IHD, who had a follow-up stress-rest myocardial perfusion SPECT (MPI) being clinically stable in medical therapy (infarction, revascularization, and changes in frequency/severity of angina were excluded) were evaluated. At the time of the study 1, the mean number of coronary risk factors was 1.8 ± 1.0 , 37% had typical angina, 32% had a previous MI, 45% had documented coronary stenoses and 33% had a previous CABG/PTCA; LVEF was preserved (>50%) in 85% of pts. All pts had a 2-day stress-rest MPI with MIBI. The regional tracer distribution on the polar map was compared with a normal gender-matched data-base: differences between studies were considered significant when the extent of perfusion defect (PD) was >5% of LV surface; ischemia was considered severe for defects reversibility >15% of LV surface and moderate when >5% and < 15%.

Results. At study 1, a rest PD was observed in 66 pts (38%) and a reversible PD was documented in 49 pts (28%). The follow-up study (study 2) was performed on average 2.7 ± 0.8 yrs after the study 1. Medical therapy in the follow-up included: NTG in 55% of pts, B-blockers in 50%, α -antagonists in 60%, and ACE-inhibitors in 20%. In all pts, the same stress of study 1 was performed (dipyridamole in 91 pts, 52%). No significant differences between study 1 and study 2 were observed in the incidence of chest pain, ischemic ECG changes, in the hemodynamic response (blood pressure and heart rate) during stress as well as in the extent of rest PD. On study 2, stress perfusion worsened in 46 pts (26%); in 10 pts the ischemic area was larger than in study 1, and in 36 pts a new reversible PD (moderate in 30/36 (83%) pts and severe in 6/36 (17%) pts) was documented. In 11 additional pts (6%), the ischemic area at study 2 reduced. A trend was observed between the number of risk factors and the worsening of stress MPI (24%, 31% and 59% in pts with >2, 2 or >2 risk factors, respectively, $p=0.03$).

Conclusions. Despite medical therapy and in clinical stability, stress MPI worsened in 26% of pts. The worsening was more frequent in pts with >2 risk factors; in this subset of pts, even if clinically stable, a stress MPI after 2 yrs could be suggested to assess CAD progression and identify pts at greater risk of events.

7.26

Prognostic value of 99Tc-tetrofosmin SPECT exercise myocardial scintigraphy after incomplete revascularization with coronary stenting.

A. R. Alfredo Galassi, C. Grasso, S. Azzarelli, E. Leotta, S. Moshiri, C. Tamburino, Ferrarotto Hospital, Cardiology Division, Catania, Italy

Backgrounds. We evaluate the prognostic value of exercise myocardial scintigraphy in patients who undergo incomplete percutaneous coronary revascularization.

Methods. In 322 consecutive patients with multivessel coronary artery disease who underwent incomplete revascularization with coronary stenting, an exercise 99mTc-tetrofosmin SPECT scintigraphy was performed prospectively 4 to 6 months after the revascularization procedure. Follow-up was defined as time from scanning until a cardiac event occurred, and lasted up to 84 months.

Results. Patients with normal scan were at low risk of cardiac events as compared to patients with mildly and severely abnormal scan (yearly event rate 1.5% vs 5.1 and 8.5%, respectively, $p<0.01$). The Kaplan-Meier survival curves showed a significant difference in hard, soft and composite event-free survival between patients with normal, mildly abnormal and severely abnormal scan ($p<0.01$, $p<0.05$ and $p<0.01$, respectively). With the use of Cox proportional-hazards analysis, nuclear data provided significant incremental prognostic value for cardiac events as compared to clinical, angiographic, and exercise test.

Furthermore, when patients were stratified on the basis of residual ischemia or myocardial necrosis found on exercise 99mTc-tetrofosmin SPECT scintigraphy, Kaplan-Meier survival curves showed a significant difference in hard event-free survival between patients with myocardial necrosis and ischemia, necrosis alone, ischemia alone or normal scan ($p<0.05$).

Conclusions. In patients with incomplete revascularization procedures exercise myocardial scintigraphy provided both significant independent information concerning the subsequent risk of cardiac events, with an annualized event rate >2% for patients with a normal scan, and an incremental prognostic information after adjusting for clinical, angiographic and exercise variables.

7.27

A prospective, multi-center trial to identify the prevalence of inducible ischemia in patients presenting with diabetes and without known coronary artery disease: preliminary results.

W. Acampa¹, A. Ferro¹, M. Petretta², M. Salvatore¹, A. Alberto Cuocolo¹ ¹Department of Diagnostic Imaging, University Federico II, Napoli, Italy, ²Department of Cardiology, University Federico II, Napoli, Italy

Aim: Coronary artery disease (CAD) is the leading cause of morbidity and mortality in patients with diabetes mellitus and these patients have an elevated prevalence of silent myocardial ischemia. This study assessed the prevalence of inducible ischemia by sestamibi SPECT in patients with diabetes without history of CAD and/or evidence of myocardial infarction.

Methods: We studied 126 consecutive patients with at least a five-year history of diabetes mellitus without history of myocardial ischemia or evidence of myocardial infarction represented on ECG. A computer program (CADENZATM, Advanced Euristic) was used to determine pre- and post-test likelihood of CAD. Beside diabetes, the program considered for analysis of pre-test likelihood of CAD the following variables: age, sex, angina symptoms classification, blood pressure, serum cholesterol, smoking history, resting ECG and family history. All patients underwent rest and dipyridamole (0.142 mg/kg/min intravenous over 4 minutes) stress sestamibi SPECT. Both rest and stress sestamibi studies were interpreted by 2 independent observers utilizing a 17-segment scoring system to determine summed stress score (SSS), summed rest score (SRS) and summed difference score (SDS). Based on this model, SPECT studies with an SRS or SSS3 were considered abnormal. The SDS was used to determine the presence of inducible ischemia and to assess the extent and severity of perfusion defects (mild, moderate and severe).

Results: On the basis of CADENZA, diabetic patients were divided into 3 groups: low (62 patients), intermediate (44 patients) and high (20 patients) pre-test likelihood of CAD. Inducible ischemia at SPECT was present in 30 patients (48%) with low, in 20 (45%) with intermediate and in 10 (50%) with high pre-test likelihood of CAD ($P=0.96$). The extent and severity of myocardial ischemia was not different in the 3 groups of patients (all $P=NS$). Taking in account SPECT results, 4/62 (36%) patients with low pre-test likelihood shifted in intermediate post-test likelihood and 30/44 (68%) patients with intermediate pre-test likelihood shifted in low post-test likelihood ($P<0.05$).

Conclusion: The preliminary results of this prospective multi-center trial, demonstrate that in diabetics without known CAD, patients with low pre-test likelihood had similar prevalence of myocardial ischemia at sestamibi SPECT imaging as compared to those with intermediate and high pre-test likelihood. In addition, they suggest that SPECT is potentially useful to add further information in assessing the likelihood of CAD in patients with diabetes mellitus.

7.28

Impact of ACC/AHA guidelines for risk stratification and management of patients undergoing vascular surgery (vs) a prospective study.

P.L. Pierluigi Pieri¹, R. Berta², G. Moscatelli³, F. Buccoliero⁴ ¹M. Bufalini Hospital, Nuclear Cardiology, Cesena, Italy, ²"Maggiore" Hospital, Division of General Surgery, Bologna, Italy, ³"M. Bufalini", Nuclear Medicine, Cesena, Italy, ⁴"Bufalini" Hospital, 2nd II Division of General Surgery, Cesena, Italy

Aim: To assess the clinical impact of the ACC/AHA Guidelines for risk stratification and management of pts undergoing vascular surgery in a prospective manner.

Methods: 201 consecutive pts (age 70.5 range 40-85) who were candidates for VS (101 carotid endo-arterectomy and 100 aortic or peripheral vascular surgery) were prospectively evaluated based on the ACC/AHA guidelines according to a risk stratification which accounting for: 1) clinical predictors of increased perioperative risk (major, intermediate and minor), 2) surgery specific risk and 3) functional capacity. Further assessment of the ischemic cardiac risk was assessed by Stress-SPECT- MPI (\pm GATED) according to the ACC/AHA Guidelines. Stress MPI images were evaluated as normal or Fixed(F)/Reversible(R)/Fixed + Rev.(FR) defects and their extent and severity.

End Points: Cardiac death, M.I., Unstable angina and CHF occurring within 30 days from surgical procedure.

Results: Clinical risk factors were present as follows: Major: 1 patient; Intermediate: 75 pts; Minor: 90 pts; No risk factors: 35 pts.

Among all patient evaluated, stress MPI was performed according to the ACC/AHA guidelines in 43 pts (21%) (Dipyridamole $n=33$; exercise: $n=10$) and was abnormal in 27 pts: F: 2 pts; R (not extensive) in 17 pts; F+R in 7 pts. In one pt ischemia was extensive. In 16 pts, MPI was normal.

Clinical management: In one patient, vascular surgery was cancelled because of his high cardiac risk; Only one patient was further evaluated with coronary angiography because of extensive ischemia.

In the remaining pts with mild/moderate ischemia, coronary angiography was not performed and medical therapy was optimized (beta-blockers).

Perioperative Outcome: None of the pts experienced cardiac death. One pt had M.I. in the perioperative phase. One pt developed unstable angina.

Conclusions: The results of this study show that in pts undergoing vascular surgery;

- 1) A risk stratification based on the rigorous application of ACC/AHA guidelines is associated with a very low risk of perioperative cardiac events (0.5% hard events and 0.5% soft events);
- 2) A selected use of stress myocardial perfusion imaging in pts at higher clinical risk improve the confidence of physicians in the management of pts with CAD;
- 3) Coronary angiography and myocardial revascularization can be avoided before vascular surgery in most of pts with CAD, when the extent of ischemia (as determined by MPI) is mild to moderate in degree and adequate medical therapy and monitoring are employed.

7.29

Incidence of post-exercise stunning evaluated by Gated-SPET myocardial perfusion imaging A Multicenter Study.

E. Inglesse¹, C. Claudio Marcassa², G. Medolago³, A. Imperiale⁴, ML. De Rimini⁵, F. Bertagna⁶, P. Sullo⁷, M. Lupo⁸, A. Ferro⁹, M. Cappagli¹⁰ ¹Ospedale della Carità, Nuclear Medicine, Novara, Italy, ²S. Maugeri Fnd IRCCS, Cardiology, Veruno, Italy, ³Gen.Hosp. Nuclear Medicine, Bergamo, Italy, ⁴Florence University, Nuclear Medicine, Florence, Italy, ⁵Monaldi H., Nuclear Medicine, Naples, Italy, ⁶Spedali Riuniti, Nuclear Medicine, Brescia, Italy, ⁷Nuclear Medicine, Caserta, Italy, ⁸Nuclear Medicine, Palermo, Italy, ⁹Un. Federico II, Nuclear medicine, Naples, Italy, ¹⁰Nuclear Medicine, La Spezia, Italy

Aim: 1) to determine the incidence of post-exercise stunning (PES) in a high risk population and, 2) to investigate the outcome of pts with PES during a 2 years follow-up.

Methods: from May 2002 to April 2004, 10 centers prospectively enrolled 498 male pts (63+7 yrs) with intermediate-to-high pre-test likelihood of CAD. Pts with LVEF 35%, advanced non-ischemic heart diseases, procedures of revascularization < 6 months or unable to reach the 85% of maximum predicted heart rate, were excluded. All pts underwent rest and exercise gated-SPECT with 99mTc-labeled agents in separate days. Regional perfusion (RP) and wall motion (RWM) in 9 myocardial segments were visually classified on a five-point scoring scale (0=normal to 4=severe); summed perfusion and wall motion scores at rest and exercise, as well as their difference, were calculated. Volumes and LVEF were calculated with commercial softwares. Data were collected on the GICN web site, and a data-base was automatically generated. Ischemia was defined as a SDS > 1; PES was defined as a decrease of more than 5 LVEF units after stress and/or a difference RWM score > 1.

Results: Dyslipidaemia was documented in 65%, hypertension 57%, diabetes 24%, smoking 43%. Previous MI was documented in 44% of pts (24% inferior, 14% anterior) and previous CABG/PTCA procedures were performed in 16% and 34% of pts, respect. Nineteen percent of pts had typical angina, 49% were asymptomatic. The EST was positive in 150 pts (32%) and negative in 199 pts (43%). On SPECT images, ischemia was found in 229 pts (49%). PES was documented in 111 pts (22%); PES was observed in 24% of pts with reversible PD and in 18% of pts without (ns). PES pts showed significant increase in EDV and a greater RWM difference score (all p<0.001). However, no differences in positive EST, hx of previous MI, CABG/PTCA were observed between pts with and without PES.

Conclusions: In a large population of male pts routinely studied for diagnostic purposes and/or risk stratification, PES was documented in 22% of pts. PES was unrelated to the presence of previous MI, ECG changes or stress-induced differences in perfusion scores. The follow-up of these pts is ongoing.

7.30

Usefulness of thallium-201 myocardial perfusion SPECT images in type 2 diabetic patients without typical chest pain.

H. Hiroshi Fukuda, T. Kunimasa, T. Furuhashi, M. Moroi. Toho University Ohashi Hospital, Division of Cardiovascular Medicine, Tokyo, Japan

Background: Diabetic patients with coronary artery disease often have no typical chest pain. The incidence of coronary artery disease in diabetic patients without typical chest pain is unknown. The purpose of this study was to investigate usefulness of Thallium (TI)-201 stress myocardial perfusion SPECT images (MPI) in type 2 diabetic patients with no typical chest pain and no prior coronary artery disease.

Methods: Consecutive type 2 diabetic patients (n =116, male =66, age= 64, asymptom =29, atypical chest pain =17, abnormal electrocardiogram =82, hemodialysis =22) were followed up for 31 months after TI-201 pharmacologic stress MPI. Follow up time was censored at the occurrence of acute coronary syndrome (ACS) or revascularization. Defect score was calculated using a 20-segment model and a 0-4 scale.

Results: SPECT images showed abnormal (defect score >3) in 23 (20%) and normal in 93 (80%) patients. ACS occurred in 3 (3%) and revascularization occurred in 5 (4%) patients. There is a significant difference in Kaplan-Meier curves between patients with perfusion defects and those with normal SPECT images (P =0.0013). Cox regression analysis was shown in Table.

Conclusions: Perfusion defect of TI-201 pharmacologic stress MPI is a good predictor of coronary events in type 2 diabetic patients with no typical chest pain and no prior coronary artery disease.

Cox regression analysis

	Hazard ratio	95%CI	P value
defect score>3	7.369	1.760-30.855	0.0063
mean washout rate<35%	2.140	0.510-8.973	0.2982
atypical chest pain	0.896	0.110-7.299	0.9185
abnorml electrocardiogram	0.746	0.178-3.125	0.6885

7.31

A selective angiotensin receptor antagonist, termisaltan, produced regression of left ventricular hypertrophy with the improvement of myocardial perfusion and fatty acid metabolism.

W. Watanabe Yasuhi¹, S. Akihiro¹, Y. Akio¹, K. Ryou¹, T. Kimio¹, W. Yasunori¹, T. Yasuhiko², E. Nariaki² ¹Hitachi General Hospital, Cardiovascular Medicine, Hitachi, Japan, ²Taga General Hospital, Internal Medicine, Hitachi, Japan

Backgrounds: Although myocardial perfusion and fatty acid metabolism are reportedly impaired in myocardial hypertrophy, but there are few reports describing the changes in myocardial perfusion and fatty acid metabolism by a selective angiotensin receptor antagonist. We investigated the nuclear scintigraphic changes with left ventricular hypertrophy (LVH) under the influence of a selective angiotensin receptor antagonist, termisaltan.

Methods: The subjects consisted of 36 patients (9 women, mean age 57.5±6.3 years) in our hospital who were diagnosed as essential hypertension with left ventricular hypertrophy (LVH) and who had not been treated with any antihypertensive medication prior to the study. Moreover, all patients underwent dual single-photon emission computed tomography (SPECT) using 123I-BMIPP and 201Tl imaging at rest and other noninvasive studies (two-dimensional echocardiography for left ventricular mass index (LVMI) analysis and BNP at rest) as well as before and after 6 months termisaltan administration. SPECT findings were graded in 17 segments on a four-point scale from 3(good) to 0(none) and assessed as a summed score (uptake score). Termisaltan was administered at a mean final dose of 10.4 ± 2.1 mg/d for over 6 months and resulted in a significant decrease of systolic and diastolic blood pressures.

Results: Systolic blood pressure significantly decreased from 150.1 ± 20.2 to 130.3 ± 9.0 (p< 0.0001), and the mean LVMI decreased significantly from 177.7 ± 49.7 to 157.3 ± 54.5 (p< 0.0001). But BNP had not decreased significantly from 112.5 ± 49.3 to 99.6 ± 41.5. Moreover, each uptake score of BMIPP and Tl increased (BMIPP: from 46.03 ± 3.0 to 47.4 ± 2.9 (p< 0.005) and Tl: from 44.9 ± 4.0 to 46.9 ± 3.2 (p< 0.005)).

Conclusion: Termisaltan produced regression of left ventricular hypertrophy with the improvement of myocardial perfusion and fatty acid metabolism. Our findings suggest that pharmacological blockade of angiotensin II receptors by termisaltan could improve LVH in never-treated essential hypertension patients, which may relate to the improvement of the improvement of myocardial perfusion and fatty acid metabolism.

7.32

Marked dispersion of cardiac FDG uptake for medical examination under fasting state by the whole body from consecutive 564 cases in Japanese.

W. Watanabe Yasuhi¹, S. Akihiro¹, Y. Akio¹, K. Ryou¹, W. Yasunori¹, T. Kimio¹, T. Yasuhiko², E. Nariaki² ¹Hitachi General Hospital, Cardiovascular Medicine, Hitachi, Japan, ²Taga General Hospital, Internal Medicine, Hitachi, Japan

Background: Positron emission tomography (PET) with 18F fluoro 2deoxy D glucose (FDG) is a non-invasive method for surveying the whole body and detecting various malignancies. And for patients with advanced ischemic heart disease, PET is a reimbursable method for identifying those suitable for revascularization. In general, under fasting state myocardial metabolism was dependent in free fatty acid. Thus, it is thought that cardiac FDG uptake had been decreased remarkably under fasting and resting state. Although cardiac FDG uptake for medical check had been found to a certain extent, there were no investigated data. The purpose of the present study is to examine the cardiac FDG uptake under fasting and resting state.

Methods: A total of consecutive 564 subjects underwent whole-body FDG PET studies in our hospital over 6 months period. All studies had been worked out under fasting over than 6 hours and enough resting before PET study. All subjects had no underlying heart disease and no previous cardiac events. And subjects with uncontrolled diabetes mellitus or over than high blood sugar level (>130 mg/dl) had been excluded. The uptake of cardiac FDG was scored semi quantitatively from 3 (equal to brain uptake) to 0 (none) in whole left myocardium (cardiac uptake score; CUS). We examined the relation analysis between CUS and the patient's characteristics (age, gender, body mass index (BMI), fasting blood sugar (FBS)).

Results: (See table)

Conclusion: Our study revealed marked dispersion of cardiac FDG uptake for medical examination under fasting state. Moreover cardiac FDG uptake is not related to BMI, FBS and subject characteristics. Recently, myocardial glucose metabolic complexities in cardiac FDG imaging had been reported. Some of them referred a measure of the rate of FDG accumulation may be just that a measure of FDG accumulation and not a measure of metabolic rate. Our findings might support their suggestions and suggest some of unknown factors in myocardial glucose utilization.

Table

	0	1	2	3
Cases(%)	252(44.7)	64(11.3)	72(12.8)	176(31.2)
BMI	23.1	22.5	23.1	23.1
FBS	96.8	99.3	98.0	98.6
Gender/Age	no differences	no differences	no differences	no differences

CUS:Cardiac uptake score BMI:Body mass index FBS:fasting blood sugar

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7.33

Parametric imaging for myocardial blood flow and perfusable tissue fraction with [O-15]water and PET.

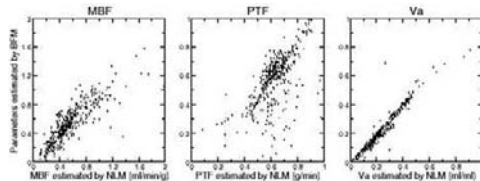
H. Hiroshi Watabe, N. Teramoto, Y. Ohta, Y. Kou, T. Hayashi, H. Iida. National Cardiovascular Center, Research Institute, Suita, Japan

[O-15]water has several advantages such as ability of repeated scan and is ideal tracer to measure blood flow. Regional MBF (myocardial blood flow) can be measured with [O-15]water and PET using one-tissue compartment model with perfusable tissue fraction (PTF), which provides MBF value that is free from partial volume effect. However, due to the short scan period and the small distribution volume of [O-15]water in the myocardium, image quality of [O-15]water is limited, which makes difficult to compute MBF value at the voxel level. We developed a method for generating parametric images of MBF, PTF and arterial blood volume (Va) with [O-15]water and PET. The method was based on basis function method (BFM) to linearize solution of one-tissue compartment model, which results in more stable and computationally much faster than conventional non-linear least squares fitting method (NLM) to estimate parameters.

In order to validate BFM, series of PET studies were performed on pigs (n=8). PET scans with [O-15]water were performed with varying doses of adenosine (5-7 scans for each pig). Myocardial region were segmented into 9 regions of interest (ROI) of myocardium regions. MBF, PTF and Va values of 9 regions for each scan were computed by BFM and NLM, and estimated parameters by two methods were compared.

The figure shows comparisons between NLM and BFM for each each regions. As shown in this figure, the estimated MBF, PTF, and Va values by BFM and NLM were highly correlated.

In conclusion, BFM is able to produce parametric images of MBF, PTF and Va with [O-15]water and PET. Parametric images could be useful to diagnose regional myocardial perfusion abnormalities.



Comparison between NLM and BFM

7.34

Prognostic factors of myocardial perfusion imaging in medically treated patients with acute myocardial infarction having nonviable myocardium.

H.S. Hee-Seung Bom, H.C. Song, J.J. Min, Y.J. Heo. Chonnam National University Hospital, Nuclear Medicine, Gwangju, Korea, Republic of

Aim: To evaluate prognostic factors of myocardial perfusion imaging in patients with acute myocardial infarction showing nonviable myocardium on myocardial perfusion imaging hence treated medically.

Methods: Subjects were 30 patients (26 males, 4 females) of acute myocardial infarction treated medically. They underwent myocardial perfusion imaging within 1 month of acute myocardial infarction attack using Tc-99m-tetrofosmin and adenosine, which showed nonviable myocardium on infarcted lesions. They were followed for 30.6 ± 15.7 months.

Results: Four cardiac events were developed including 2 cardiac deaths and 2 recurrent myocardial infarctions. Univariate analysis showed uptake of infarct area ($P=0.03$) and size of necrotic area ($P=0.05$) as significant prognostic factors. Multivariate analysis showed that uptake of infarct area was the only significant factor.

Conclusion: Lower uptake in nonviable myocardium is related to poor prognosis in medically treated patients with acute myocardial infarction having nonviable infarction.

7.35

Prognosis of patients with positive exercise test and normal myocardial perfusion SPECT.

JH. Seo¹, J. Jae-Tae Lee¹, JH. Bae¹, SY. Jeong¹, BC. Ahn¹, SC. Chae², KB. Lee.¹
¹Kyungpook National University Hospital, Nuclear Medicine, Taegu, Korea, Republic of, ²Kyungpook National University Hospital, Cardiology, Daegu, Korea, Republic of

BACKGROUND: Exercise SPECT myocardial perfusion imaging (Ex-MPI) is regarded as a critical predictive technique in patients with coronary artery disease (CAD) particularly who have higher-function capable of performing exercise testing. But sometimes in clinical practice, we encounter equivocal situations of discordant findings between exercise ECG and MPI. In current study we evaluated the prognosis of subjects with positive ECG and normal MPI findings, and predictive factors for future cardiac events were also studied.

METHOD AND SUBJECTS: A total of 2571 Ex-MPI studies were reviewed over a period of 3 years. Subjects were followed for more than 2 years (24-56 months, mean 35months) for cardiac events after exercise testing. The cardiac events were defined as hard events (cardiac death and nonfatal myocardial infarction (MI)) and soft events (aggravation of CAD necessitating revascularization, severe congestive heart failure necessitating hospital admission for treatment). We have evaluated age, sex, typical angina pain, rest ECG abnormalities, hypertension, diabetes mellitus (DM), serum levels of cholesterol and LDL, smoking history, history of cerebrovascular disease (CVD) and peripheral artery disease (PAD), and rest left ventricular ejection fraction (LVEF) as clinical variables.

RESULTS: Of 83 subjects with positive ECG and normal MPI findings, 6 were considered as false negative results confirmed with coronary angiography at the time of MPI study. There were 77 patients (mean age 52years, 39 males and 38 females) with positive ECG and normal MPI results. During the follow-up period, there were 3 cardiac events (event rate 1.9% per year, no cardiac death but 2 nonfatal MIs (event rate 1.3% per year) and 1 soft event (event rate 0.6% per year) out of 77 studies. 2 patients out of 39 males (5.1%), and 1 out of 38 females (2.6%) had cardiac events. All cardiac events were observed within 2 years. 1-year cardiac event rate was 0.6% (1 event during the first year) and 2-year cardiac event rate was 1.9% (3 events during 2 years). Among clinical factors, male sex, typical chest pain and smoking history at the time of MPI were predictive of cardiac events.

CONCLUSION: Patients with positive ECG and negative Ex-MPI results have very low risk for cardiac events. Nevertheless, the cardiac events cannot be excluded totally in some cases.

7.36

Detection of myocardial ischemia with myocardial perfusion SPECT in patients with diabetes mellitus.

JH. Seo¹, J. Jae-Tae Lee¹, JH. Bae¹, SY. Jeong¹, BC. Ahn¹, SC. Chae², KB. Lee.¹
¹Kyungpook National University Hospital, Nuclear Medicine, Taegu, Korea, Republic of, ²Kyungpook National University Hospital, Cardiology, Daegu, Korea, Republic of

BACKGROUND: Diabetes mellitus (DM) is a critical disease associated with higher rates of cardiovascular morbidity and mortality. Atherosclerosis accounts for 65-80% of all deaths in diabetic patients and patients with DM are known to show high prevalence of coronary artery diseases (CAD). In current study we have evaluated the incidence of scintigraphic evidence of CAD in diabetic patients and results were compared with cardiovascular symptoms and clinical factors.

METHOD AND SUBJECTS: 169 patients with DM (mean age 62 years, 68 males and 101 females) were referred for evaluation of CAD between January 2002 and December 2003. 101 (60%) patients were with chest pain and 68 (40%) were asymptomatic. Patients underwent exercise (n=6) or adenosine stress (n=163) SPECT myocardial perfusion imaging (MPI). Exclusion criteria included history of documented myocardial infarction, prior revascularization, clinically significant valvular heart disease, left-bundle branch block on rest ECG. We evaluated symptoms associated with cardiac problem as well as other clinical and laboratory data to reveal correlation with presence of CAD. Tomographic images were assessed visually and semi-quantitatively with C-Equal program.

RESULTS: Myocardial ischemia was detected in 52 (31%) patients. Among them, 41 had 1-vessel disease and 9 had 2-vessel disease. In 52 patients with ischemia, 28/52 (54%) were male and 24/52 (46%) were female. 20/68 (29%) asymptomatic patients and 32/101 (32%) symptomatic patients had ischemia on MPI. Higher prevalence of neuropathy, hypertension, higher blood glucose level, HbA1c and CRP was noted in patients with myocardial ischemia. Serum levels of cholesterol and LDL was not significantly different between patients with ischemia and with normal MPI findings. Abnormal MPI findings were not related with gender and age.

CONCLUSION: These results show a high prevalence of abnormal MPI results in diabetic patients regardless of symptoms. Screening stress MPI in diabetic patients should be indicated irrespective of symptoms, especially in patients with diabetic neuropathy, hypertension, higher level of blood glucose, or increased CRP.

7.37

Assessment of left ventricle perfusion with Tc-99m-MIBI SPECT and RNV in patients with AMI treated with bone marrow stem cells.

M. Malgorzata Popiel¹, S. Grajek¹, R. Czepczynski², P. Breborowicz¹, M. Lesiak¹, A. Czyn³, K. Sawinski³, M. Komarnicki³, A. Cieslinski¹, J. Sowinski² ¹Institute of Cardiology, First Department of Cardiology, Poznan, Poland, ²Department of Endocrinology, Poznan, Poland, ³Department of Haematology, Poznan, Poland

Aim of the study: assesment of left ventricle perfusion (LVP) in patients (pts) with AMI treated with BMSC autotransplantation.

Material and Methods: pts with first anterior wall AMI in whom LAD occlusion was diagnosed, who were successfully treated with primary/rescue PCI and who gave informed consent, were enrolled to the trial. A 5-7 day pts received autologous transplantation of CD34+/AC133+ BMSC via infarct related artery (IRA); 14 pts were treated with BMSC and 7 pts in control group so far, as the trial is ongoing. LVP was obtained with Tc-99m-MIBI SPECT performed at 3-4 day and after every 3 months. Radioisotope ventriculography (RNV) was performed at 7 (7-10) day and after 6 months. Semiquantitative Tc-SPECT analysis was based on 5 points scale of tracer uptake and 16-segmental model of left ventricle which served to calculate perfusion index (PI; PI=[sum of points × 16 seg]/16).

Results: age, maximal CPK, sum of ST segment elevation and ST resolution, time pain-to-needle, TIMI 3 rate, MBG, cTFC after PCI and infarct size approximated by echo (contractility index) did not differ in both groups. LVP index was better in pts treated with BMSC, although small number of pts excludes statistical analysis at a moment (table 1). RNV results: mean EF at 7 day was 48% in treated group (14 pts) and 45% after 6 months (6 pts so far), and 41% at 7 day (7 pts; NS to 48% in treated group) and 37% after 6 months in control group (3 pts so far).

Conclusion: perfusion of left ventricle assessed with Tc-99m-MIBI SPECT in pts treated with BMSC seem to be better than in control group, although further results of ongoing follow-up are warranted to confirm the data and enable statistical analysis.

Table 1.

pts	4 day	3 mo rest	3 mo dip	6 mo rest	6 mo dip
Treated/n	2,366/14	2,227/12	2,176/12	2,260/7	2,145/7
Control/n	2,482/7	2,68/5	2,712/5	2,895/2	3,194/2

7.38

Concomitant anti-ischemic medication does not affect the prognostic value of a normal stress myocardial perfusion test.

A. António Ferreira, A. Ventosa, V. Gil, J. Calheiro, S. Lima, C. Aguiar, R. Couto, L. Raposo, R. Seabra-Gomes. Hospital de Santa Cruz, Cardiology Department, Carnaxide, Portugal

Background: Whether antianginal medication affects the prognostic value of a stress myocardial perfusion imaging test remains a controversial issue. Our hypothesis was that in patients with a normal single photon emission computed tomography (SPECT) stress test, outcome would be worse in those whose test was performed on anti-ischemic medication.

Methods: We retrospectively studied 352 consecutive patients with a normal stress myocardial perfusion SPECT. The study endpoint was time to a major cardiac event (cardiac death or non-fatal myocardial infarction).

Results: Previously documented coronary artery disease (CAD) was present in 79 patients (22.4%). Stress consisted of an exercise treadmill test in 233 tests (66.2%). At the time of testing, 71 patients (20.2%) were on beta-blocker therapy, 82 (23.3%) on calcium channel blockers, and 57 (16.2%) on nitrates. During a median follow-up of 4.8 years (range, 1.4 to 76.1 months), 12 patients (3.4%) suffered a major cardiac event (7 non-fatal myocardial infarctions and 5 cardiac deaths). Time to a major cardiac event was similar regardless of whether or not the test was performed under the effect of an anti-ischemic drug: event-free survival at last follow-up was 100% vs. 95.7% for beta-blockers, 93.9% vs. 97.4% for calcium channel blockers, and 94.6% vs. 96.9% for nitrates (log rank p=ns for all comparisons). Independently of the presence or absence of known CAD, performing the test under any anti-ischemic medication did not influence outcome, even after adjustment for other variables (age, gender, CAD risk factors, presence of left bundle branch block, and type of stress).

Conclusion:

A normal stress SPECT performed under anti-ischemic medication remains a strong indicator of good prognosis.

7.39

Myocardial perfusion imaging in patients with chest pain and nonsignificant angiographic lesions-correlation to biochemical markers of myocardial injury.

M. Mariana Vasconcelos¹, E. Martins², T. Faria³, A. Oliveira³, M. Garcia², J. Pereira³, F. Rocha-Gonçalves² ¹São João Hospital, Cardiology, Porto, Portugal, ²São João Hospital, Cardiology, Porto, Portugal, ³São João Hospital, Nuclear Medicine, Porto, Portugal

Background: In patients with chest pain and hemodynamically significant coronary lesions myocardial perfusion imaging (MPI) has been shown to provide diagnostic information. Less studies have explore the diagnostic potencial of MPI in patients with stenosis involving 50% of the coronary lumen, generally considered to have no hemodynamic significance.

The aim of this study was to evaluate the results of MPI in these patients and to correlate them to Troponin I (TnI), a sensitive marker of myocardial injury.

Methods: We enrolled 40 patients (19 male), mean age 56.4 years, without a prior myocardial infarction admitted in our hospital department for chest pain. The initial assessment included ECG and serum TnI levels (twice with a 6 hour lag). All patients underwent coronary arteriography (CA) that revealed nonsignificant (<50%) angiographic lesions. SPECT MPI was performed with 99m-Tc tetrafosmin 28.8 ± 37.3 days within CA. Treadmill exercise was used in 13 and pharmacologic stress in 27 patients. Regarding the results of TnI levels, 2 groups were established: I-Negative TnI (n=18); II-Positive (>0,1ng/ml) TnI (n=22).

Results: Of the 40 patients, 26 (65%) had a normal SPECT MPI and 14 (35%) had an abnormal study, including 5 (13%) patients with fixed defects and 9 (22%) patients with reversible defects. We found no correlation between serum TnI levels and perfusion defects.

The percentage of normal results was similar in both groups, as shown in table 1. In patients with negative TnI (group I) we observed a higher incidence of ischemia (reversible defects).

Conclusion: In patients with chest pain and nonsignificant angiographic lesions there is a high percentage of abnormal MPI results. The rise of TnI can not predict an abnormal study in this group of patients.

Table 1.

MPI	Group I (n=18)	Group II (n=22)
Normal	61% (11/18)	68% (15/22)
Abnormal	39% (7/18)	32% (7/22)
Fixed Defect	11% (2/18)	18% (4/22)
Reversible Defect	27% (5/18)	14% (3/22)

7.40

Evaluation of perfusion defect and ventricular function in patients with Q wave and non Q wave myocardial infarction.

C. Cândida Lourenço¹, C. Roque², A. Ferrer-Antunes¹, M. Ferreira², L.A. Providência², J. Lima¹ ¹Coimbra's University Hospital, Nuclear Medicine, Coimbra, Portugal, ²Coimbra's University Hospital, Cardiology, Coimbra, Portugal

Aim: The aim of this study was to assess the effect of Q wave and non Q wave infarction in perfusion defects and ventricular function.

Methods: Sixty nine patients (54 men, 15 women, mean age of 63.4 ± 12 years) with a previous myocardial infarction performed a one day stress-rest 99mTc-Tetrafosmin myocardial perfusion scintigraphy. According to the electrocardiogram (ECG) pattern two groups of patients were considered: 37 patients with Q wave pattern and 32 patients without the presence of Q waves. A semi-quantitative analysis of perfusion images was performed using a 17 segment model based in 3 sections (apical, medial and basal) of the short axis and in a section of the vertical long axis representing the apex. Overall perfusion scores [stress score (SS), rest score (RS) and difference score (DS)] were calculated. Rest left ventricular ejection fraction (LVEF), left ventricular (LV) end systolic volume and LV end diastolic volume were assessed by Cedars quantitative gated SPECT. A SS greater than 8, a multivessel perfusion abnormality, a LVEF lower than 45% or a LV end systolic volume higher than 70ml were considered as scintigraphic high risk factor. Quantitative variables were described as mean ± sd deviation and ANOVA was used to compare.

Results: Significant higher SS and RS, lower LVEF and higher LV volumes were obtained in patients with Q wave ECG pattern. There was no significant difference between the groups in the DS. Ninety two percent of patients with Q wave ECG pattern had at least one scintigraphic high risk factor; only 34% of patients with non Q wave pattern had a scintigraphic high risk factor.

Conclusions: Patients with Q wave infarction had significantly more extensive and severe stress and rest perfusion defects, more depressed LV function and higher LV volumes. The area of ischemia was similar in both groups.

ANOVA Comparison of groups

	Q wave ECG pattern	Non Q wave ECG pattern	p value
Stress score	19,3 ± 7,4	13,9 ± 6,9	0,0028
Rest score	14,9 ± 7,8	7,87 ± 5,5	<0,0001
Difference score	4,3 ± 4,4	5,75 ± 4,2	0,178
LVEF	46,2 ± 15,4	58,6 ± 12,1	0,0087
LV end systolic volume	94,2 ± 66,3	52 ± 40,3	0,025
LV end diastolic volume	158,5 ± 70,6	115,6 ± 49,7	0,038

7.41

Diagnosis of CAD at patients with systemic hypertension using myocardial perfusion imaging SPECT-99m Tc tetrofosmin.

C. Claudia Medrea¹, R. Bogdan², A. Lazar², S. Mot², R. Capilneanu.² ¹Heart Institute "N. Stancioiu", Nuclear Cardiology, Cluj-Napoca, Romania, ²Heart Institute, Cardiology Dept., Cluj-Napoca, Romania

Purpose: To compare the accuracy of exercise stress 99m-Tc Tetrofosmin (Myoview) SPECT for the diagnosis of CAD in patients with and without systemic hypertension (HBP).

Subjects and Methods: 60p (age 54 ± 10 years; 49 males 11 females); 25p with HBP and 35p without HBP were included in the study.

The MPS SPECT stress test, protocol Bruce 99m-Tc Myoview was performed during the first day, and the rest MPS SPECT 99m-Tc Myoview was acquired 24 hours after the stress MPS.

All patients were without previous myocardial infarction.

Significant CAD was defined as >50% luminal diameter stenosis in one or more major coronary arteries at the coronarography.

LVH criteria at echocardiography: IVS=11-15 mm ;PW=11-15 mm

Results: * In patients with HBP, the myocardial perfusion abnormalities (MPA) were detected in 17 of 22p with significant CAD, and 1 of 3p without significant CAD.

* In patients without HBP, MPA were detected in 19 of 27p with significant CAD, and 2 of 8p without significant CAD.

* There was no difference between patients with and without HBP regarding sensitivity, specificity and accuracy of exercises stress 99m-Tc Myoview SPECT for the diagnosis of CAD in the two groups, respectively 77% vs. 73% ; 73% vs. 70%; 75% vs. 72% ;p=NS

* LVH was detected in 43% of patients. No significant difference was detected between patients with and without LVH regarding sensitivity, specificity and accuracy of exercise stress 99m-Tc Myoview SPECT for the diagnosis of CAD.

Conclusion: The exercise stress 99m-Tc Myoview SPECT imaging is a useful method for the diagnosis and localization of CAD in hypertensive patients, with an accuracy comparable with that in patients without hypertension.

7.42

Angiotensin-converting enzyme gene polymorphism adds risk for the severity of coronary atherosclerosis.

V. Vickenty Kozulin, O. Berkovich, T. Ivashchenko, V. Larionova, I. Espipovich, M. Gordeev, A. Panov, E. Shlyakhto. St. Petersburg, Russian Federation

Purpose: to investigate the relation between the angiotensin-converting enzyme (ACE) gene polymorphism and severity of coronary atherosclerosis, we analyzed the association of genotype with the coronary angiography findings of patients with coronary artery disease (CAD).

Methods. We determined the ACE genotype in 102 Russian patients with CAD and 112 healthy individuals. The genotype distributions were not different between two groups (p=0.48; Chi-square test). In the first group, coronary angiograms were evaluated by criteria based on the number of stenotic lesions (60% and more), the priority level of lesion (proximal or distal) and the type of lesion (diffuse or discrete).

Results. We failed to determined any significant differences between patients with DD and combined ID or II genotypes based on the priority level of coronary artery lesion (p=0.285). Although the occurrence of diffuse coronary artery lesion was higher among patients with the DD genotype than in those with the ID or II, the differences did not reach the level of significance. There were significant differences in the number of stenotic vessels among groups of patients with DD or II and ID genotypes (p=0.043) with prevalence of three vessel lesion in patients with the DD genotype. Having divided all patients on two groups with single and three vessels lesion we found that patients with the DD genotype significantly more frequently had three vessels lesion than those with the ID or II genotypes (48% vs 21.9%, respectively; p=0.023).

Conclusions. The results indicate the influence of ACE gene polymorphism on severity of coronary atherosclerosis, based on this data we may propose that CAD patients with the DD genotype have more extended coronary atherosclerosis in comparison with patients having ID or II genotypes.

7.43

MinK gene polymorphism and risk paroxysmal atrial fibrillation in the patients with sick sinus syndrome.

N. Burova, O. Berkovich¹, V. Larionova², D. Baranov², V. Timoshin², E. Shlyakhto¹. ¹St. Petersburg, Russian Federation, ²Pavlov State Medical University, St. Petersburg, Russian Federation, State Pediatric Medical Academy, St. Petersburg, Russian Federation.

Aim. To study the association of the MinK gene polymorphism with risk of paroxysmal atrial fibrillation (AF) in the patients with sick sinus syndrome (SSS).

Material and methods: Two hundred eighteen patients with SSS were examined: The electrocardiography, Holter monitoring exercise test, electrophysiological study with medical autonomic denervation, pharmacological tests, and echocardiography were performed at the background of the sinus rhythm. The patients were followed up for 5 years or more. According to the clinical course of the disease, all patients were divided into 2 groups, as follows:

1. Group I, 108 patients with SSS without paroxysmal AF (43 men, 65 women, mean age 68 ± 1 year).

2. Group II, 110 patients with SSS and paroxysmal AF (34 men, 76 women, mean age 72 ± 1 year). The MinK gene genotypes (38G/38G, 38S/38S, 38G/38S) identification was carried out with use of polymerase chain reaction with subsequent restriction analysis. Fisher's Exact Test was used for the statistical analysis.

Results: The MinK 38G allele was found more frequently than the MinK 38S allele in all groups (38G I = 51.46%; 38G II = 64.55%). The odds ratio (OR) for paroxysmal AF in patients with 1 MinK 38G was 1,79 (95% CI 1,22 — 2,63), with compared in patients with MinK 38S allele. In the patients of group I and II, the 38G/38S genotype of MinK gene was found the most frequently (table 1). The OR for paroxysmal AF in patients with 38G/38G genotype of MinK gene was 2,25 (95% CI 1,24 — 4,07) when compared with patients with others MinK genotypes (38S/38S and 38G/38S).

Conclusion: The association between the MinK 38G allele and paroxysmal atrial fibrillation in patients with sick sinus syndrome was found. An increased risk of paroxysmal atrial fibrillation in patients with 38G/38G genotype of MinK gene was shown.

Table 1.

Group	38G/38G (1)	38S/38S (2)	38G/38S (3)	p (1/2)	p (1/3)	p (2/3)
I	24 (22.2%)	23 (21.3%)	61 (56.48%)	0.869	<0.001	<0.001
II	43 (39.09%)	11 (10%)	56 (50.91%)	<0.001	0.078	<0.001

7.44

The use of phenotype characteristics in mutation analysis of families with long QT syndrome.

S. Chuprova, M. Shkolnikova¹, E. Zaklyazminskaya², A. Poliakov². Center of Children's Arrhythmias, Moscow, Russian Federation¹ Center of Children's Arrhythmias, Moscow, Russian Federation², Research Center of Medical Genetics, Moscow, Russian Federation

The long QT syndrome (LQTS) is a cardiac disorder characterized by a prolonged QT interval and life-threatening tachyarrhythmias, which may give rise to recurrent syncope or sudden cardiac death. 70 unrelated Russian families were clinically evaluated using family and medical histories (including age at the first syncope and symptom related triggers of proands and their relatives), ECGs, Holter recordings with the heart rate variability (HRV), exercise test (treadmill), the efficacy of beta-blocking drugs and Na⁺ channel blockers. We have tested all of the patients for mutation in 5 genes: KCNQ1 (exons 2,4,5,6,7,14), KCNH2 (exons 2,6,7,10), SCN5A (exon 17), KCNE1 and KCNE2 using PCR-SSCP analysis and then direct sequencing. Mutations were founded in 35 families (50%): KCNQ1 in 26 families, KCNH2 in 6 families, SCN5A in 1 family and KCNE1 in 1 family. In one family (one patient) were founded mutations in 2 genes (KCNH2-W585C and KCNE1-V1071). Using ECG features exclusively 66% of the genotyped cases were predicted correctly (patients with KCNH2 mutations have more high per cent). Using ECG and other phenotype-genotype correlations 91% of all (35 families) genotyped cases were predicted correctly. Patients with KCNQ1 mutations have an early age at the first syncope, but not patients with KCNH2 mutations (6,1±3.6 and 13,6±7.4 years respectively, P<0.05). In patients with KCNH2 mutations arrhythmic syncope often occurred in association with emotional and especially acoustic stimuli, in patients with KCNQ1 mutations with exercises, the combination of exercises and emotional stress and especially swimming. The QTc was significantly prolonged during exercise in patients with KCNQ1 mutations (509,6±53,4 ms and 545,2±46,1 ms respectively, P<0,05) but not in patients with KCNH2 mutations. Some HRV parameters (time-domain) were differences between patients with KCNQ1 and KCNH2 mutations. In patients with KCNQ1 mutations beta-blockers were effective in more high doses than in patients with KCNH2 mutations. Conclusions: Using ECG and other phenotype-genotype correlations 91% of all genotyped cases were predicted correctly. The prediction of most eligible gene may be based on phenotype-genotype correlations and must determine screening strategies in families with LQTS.

7.45

Evaluation of stem cell therapy in patients with acute myocardium infarction using radionuclide methods.

S. Svetlana Sazonova, V.I. Chernov. Inst. of Cardiology, Nuclear Medicine, Tomsk, Russian Federation

Aim. The aim was to assess therapeutic effect of stem cells in patients with acute myocardial infarction using radionuclide methods.

Methods and patients. We examined 10 pts with acute myocardial infarction (MI) who were treated by intracoronary infusion of autologous stem cell (ASC) into the infarct-related artery. To track transplanted ASC in myocardium we labeled part of them using 40-60 mCi of 99mTc-HMPAO. Whole-body scans were performed at 30min, 2h and 24h post injection, following by calculation of radioactivity percentage in the heart to total radioactivity.

In order to evaluate long-term effect of ASC transplantation on myocardium we also performed SPECT with 199Tl-chloride on the terms of 2 weeks and 6 months after ASC transplantation in the same group. The presence, character and size of perfusion defects were estimated.

Results. As a result of our study in myocardium of examined patients at 30min remained 4.7±1.2% of labeled ASC, at 2h-2.5±0.4% and 24h-1.9±0.2% of total 99mTc-HMPAO-ASC. SPECT with 199Tl-chloride showed that the average size of stable perfusion defects at 2 weeks after ASC transplantation was 28.76±3.57% and after 6 month decreased up to 21.69±3.58% (p=0.01).

In the same time we observed improvement of clinical signs of the disease on the term of 6 month, including changes of NYHA functional class from 1.4±0.5 to 1.2±0.4 and of left ventricle ejection fraction from 44.2±11.5% to 50.5±5.0%.

Conclusion. Our results showed that the largest number of transplanted ASC remains in the myocardium of patients with MI. It was also confirmed that such kind of therapy provides positive effect on the myocardium perfusion. However, it is not still clear either perfusion improves due to direct action of transplanted cells or as a result of their mediate influence on adjoining tissues.

7.46

Gated SPECT abnormalities and risk factors in patients with symptomatic intracranial atherosclerotic stenosis.

G. Romero-Farina, J.F. Arenillas, J. Candell-Riera, S. Santiago Aguadé-Bruix, G. De Leon, CA. Molina, P. Chacon, J. Montaner, A. Rovira, J. Alvarez-Sabin. Vall d'Hebron, Nuclear Medicine, Barcelona, Spain

Aim of the study. The relationship between intracranial large-artery atherosclerosis (ILA) and coronary artery disease (CAD) remains unsettled. We aimed to investigate the prevalence of myocardial ischemia in symptomatic ILA-patients and to detect the factors that are associated with its presence.

Methods. Forty-nine first-ever patients with symptomatic ILA (mean age: 65 ± 8 years, 14 female) without history of CAD underwent a maximal-exercise 99mTc-MIBI myocardial gated-SPECT (one day stress-rest study). Thirty-one patients had medical history of hypertension, 35 hypercholesterolemia, 24 were cigarette smokers and 21 diabetes mellitus. Thirty-one patients presented an ischemic stroke and 18 a transient ischemic attack. In the cranial magnetic resonance imaging (angiographic sequences) 130 intracranial stenosis were observed. Lipoprotein (a) (Lp(a)), C-reactive protein, and homocysteine (Hcy) levels were determined previous to SPECT. Twenty-one patients had 3 risk factors (RF), 18 two, and six had one. Twenty-eight patients performed a symptom-limited exercise test (ET), in 14 patients dipyridamol was administered during submaximal exercise, and seven underwent dipyridamol stress test.

Results. Gated-SPECT showed reversible myocardial perfusion defects in 21 (43%) patients and fixed defects in three patients. Eleven patients developed a horizontal download of the ST segment more than 1 mm during the exercise test and two presented angina. Univariate analysis showed that males (p=0.05), diabetes (p=0.02), >2 vascular risk factors (p=0.006), asymptomatic cervical internal carotid artery (ICA) lesions (p=0.04), multiple intracranial stenoses (p=0.03), intracranial ICA stenosis (p=0.02), high Hcy levels (p=0.01) and high Lp(a) levels (p=0.04), were significantly associated with myocardial ischemic defects. A multiple logistic regression model identified >2 risk factors (OR 5.85, 95% CI 1.37-24.96, p=0.016), intracranial ICA stenosis (OR 5.51, 1.09-27.7, p=0.03) and high Hcy (OR 7.73, 1.43-41.85, p=0.017) as independent markers of myocardial ischemia.

Conclusions. Patients with symptomatic ILA stenosis have a high prevalence of myocardial ischemia in the gated SPECT. The presence of more than two risk factors, high Lp(a) levels, high Hcy levels, and location of the symptomatic stenosis in intracranial vertebral-basilar arteries could characterize patients as higher risk of CAD.

7.47

Caffeine decreases coronary flow reserve in CAD patients.

M. Mehdi Namdar¹, P.T. Siegrist², R. Grathwohl², R. Delaloye², P. Koepfli², CA. Wyss², PA. Kaufmann.² ¹Zurich, Switzerland, ²Cardiovascular Centre, Nuclear Cardiology University Hospital, Zurich, Switzerland

Purpose: Caffeine competitively antagonizes adenosine-induced hyperemic myocardial blood flow (MBF). We studied the acute impact of caffeine on exercise-induced hyperemic MBF response in coronary artery disease (CAD) patients.

Methods: 15O-labelled H2O and Positron Emission Tomography (PET) was used to measure regional MBF in 9 patients with CAD (mean age 58y ± 9) at rest and using supine bicycle exercise stress (mean workload 98% of predicted) before and 50 minutes after oral ingestion of caffeine (200mg). Hyperemic MBF of stenotic segments was expressed as percentage of hyperemic MBF in remote segments representing an index of relative flow reserve.

Results: Caffeine levels were zero at baseline in all subjects and increased to 18 ± 9mmol/l fifty minutes after caffeine intake. Neither rate pressure product (rest and exercise) nor resting MBF were affected by caffeine. By contrast, hyperemic MBF was significantly decreased in remote (2.6±0.9 to 2.0±0.7 ml/min/g, -23%; p<0.05) and even more pronounced in stenotic segments (2.4±0.6 to 1.6±0.72 ml/min/g -33%, p<0.005). Relative flow reserve decreased from 92% to 80%.

Conclusions: Caffeine consumption at an equivalent dose of two cups of coffee severely decreases hyperemic MBF response to exercise in patients with CAD. The decrease in relative flow reserve indicates that the adverse effect of caffeine is specifically pronounced in the stenotic segments, where poststenotic adenosine-mediated dilative compensatory mechanisms of the microcirculation seem to be particularly prone to the antagonistic effect of caffeine.

7.48

Impact of myocardial perfusion scanning with 13N-ammonia PET and revascularization on long-term prognosis in patients with coronary artery disease.

N. Bartenstein¹, J. Hellermann², P. T. Patrick Siegrist¹, M. Namdar¹, P. Koepfli¹, C. Pollack¹, U. Schurr³, P.A. Kaufmann.¹ ¹University Hospital Zurich, Nuclear Cardiology, Zurich, Switzerland, ²University Hospital Zurich, Cardiovascular Center, Zurich, Switzerland, ³University Hospital Zurich, Cardiac Surgery, Cardiovascular Center, Zurich, Switzerland

Background: Very limited data exist on the long-term prognostic impact of PET myocardial perfusion scan with 13N-ammonia.

Aim: To assess the impact of myocardial perfusion scanning with PET and revascularization (revasc) on long-term prognosis in patients with coronary artery disease (CAD).

Methods: The baseline characteristics and the follow up (f/u) of 68 consecutive patients (age 59±10 years) with ischemic LVD who underwent FDG and NH3 PET scan for assessment of hibernating myocardium (=NH3/FDG mismatch) was assessed. Patients were assigned according to the PET findings into hibernating and no hibernating.

Results: see table 1

Conclusion: Our results demonstrate a strong association between ischemia as detected by PET and improved survival after revascularization in ischemic patients. This association is not confined to short term follow up but is even more pronounced in the 5-year mortality. PET seems to predict correctly those who benefit most from revascularization procedure.

Table 1.

	Ischemia	Ischemia	No Ischemia	No Ischemia
	Revasc	No Revasc	Revasc	No Revasc
n	10	13	13	32
gender, male	87%	82%	83%	88%
mean f/u, years	6.5±2.1	4.7±3.1	5.3±2.8	5.1±3.3
first year mortality	10%	15%	15%	22%
5-year mortality	20%	54%	46%	41%
Survivors, end of f/u	70%	46%	45%	55%

TUESDAY
MAY
10

7.49

Normal myocardial perfusion SPECT in patients with relevant coronary stenoses in whom does it occur?

M.J. Michael Zellweger¹, P.C. Burger¹, J. Mueller-Brand², M.E. Pfisterer.¹ ¹University Hospital, Cardiology Department, Basel, Switzerland, ²Basel University Hospital, Nuclear Medicine Dept., Basel, Switzerland

Background: Myocardial perfusion SPECT (MPS) provides excellent diagnostic and prognostic information in the evaluation of coronary artery disease. However, normal MPS sometimes occur despite relevant stenoses on coronary angiograms (cath). Little is known about predictors of relevant stenoses (RS) in patients with normal MPS. The aim of this study, therefore, was to evaluate predictors of RS in patients with normal MPS.

Methods: A consecutive series of 182 patients with normal MPS referred for cath was evaluated. All patients underwent rest Tl-201/stress Tc-99m sestamibi MPS. MPS were interpreted using a 20 segments' model and a scale of 0 to 4. Summed scores were calculated by adding the 20 SPECT segment scores. Summed rest (SRS), stress (SSS) and difference scores (SDS) were derived. A normal MPS was defined by SSS < 4 and SDS < 2. A stenosis of $\geq 75\%$ assessed visually by cath was considered relevant.

Results: Out of 182 patients (36% female, mean age $62.5 \pm 10.3y$) with normal MPS, 70 (38%) had RS on cath. In 80% of these patients, only distal coronary segments were diseased. Patients with RS were older (66 ± 11 vs $60 \pm 10y$; $p=0.001$), more often reported angina during stress testing (31% vs 17%; $p=0.029$), reached lower peak watts (108 ± 50 vs 126 ± 54 ; $p=0.038$) and peak heart rates (122 ± 29 vs 136 ± 30 ; $p=0.003$), and more often had transient ischemic dilation (TID) (7% vs 1%; $p=0.029$) than patients without RS. Of note, there was no difference of antiischemic medication during stress testing between the 2 groups. Importantly, patients with triple vessel disease more frequently demonstrated TID than patients with 0,1, or 2-vessel disease, 10% and 2%, respectively; $p=0.031$). In the multivariate logistic regression analysis only age (OR 1.05, 95% CI 1.02-1.09; $p=0.004$) and angina during stress testing (OR 2.15, 95% CI 1.03-4.48; $p=0.041$) were significant and TID borderline significant (0.096) predictors of RS.

Conclusions: In a population referred for cath, 38% of patients with normal MPS had RS on cath. In 20% of these patients, i.e. in only 8% of the overall patient population, RS were located in proximal coronary segments. Furthermore, patients with triple vessel disease more often demonstrated TID than patients without triple vessel disease. Thus, elderly patients with angina during stress testing and patients who eventually demonstrate TID tend to have RS even when myocardial perfusion was normal.

7.50

Significance of ST elevation on stress myocardial perfusion scans (MPI) in women.

L. Leonie Gordon¹, A. Epps², S. Chiarameda.² ¹Medical University of South Carolina, Nuclear Medicine, Charleston, SC, United States, ²Medical University of South Carolina, Cardiology, Charleston, SC, United States

Introduction: Both positive and negative treadmill exercise tests in women have a relatively low predictive value for significant coronary artery disease. The prognostic value of stress induced ST-segment depression in women has been reviewed; however there is limited data on the significance of ST-segment elevation. Furthermore there is evidence that patients with ST-segment elevation on stress ECG coupled with reversible perfusion defects on MPI are likely to benefit from cardiac intervention. In this study, we analyzed the occurrence and significance of ST-segment elevation in a large group of women undergoing stress MPI.

Methods: We did a retrospective analysis on stress MPI tests on 4,357 women from October 1997 to September 2003 performed for routine clinical indications. Stress tests were done with exercise (Bruce or modified Bruce) or pharmacologically with either adenosine, dipyridamole or dobutamine infusion. MPI was performed with Thallium-201 and/or Technetium-99m sestamibi or tetrofosmin SPECT. Stress ECGs were analyzed and ST-segment elevation was reported if there was at least 1mm of elevation from baseline in at least two contiguous leads. Myocardial defects were reported according to standard ASNC criteria. We then reviewed how many of these women underwent left heart catheterization and the significance of these findings. Significant flow limiting coronary artery disease was defined as greater than a 70% stenosis of the coronary lumen diameter.

Results: In review of stress ECG changes ST-segment elevation was identified in 74 out of 4,357 females (1.7%). MPI analysis demonstrated that 16 out of these 74 women (22%) had reversible perfusion defects. Of these 16 women with reversible perfusion defects, 4 underwent dobutamine, 4 adenosine or dipyridamole and 8 underwent exercise stress. 11 out of these 16 female patients (69%) underwent left heart catheterization and all 11 had critical flow limiting lesions amenable to intervention or surgery.

Conclusions: We found that ST-segment elevation on stress ECG is less prevalent in females. Furthermore ST-segment elevation on stress ECG is less likely in females to be associated with a reversible perfusion defect on MPI (22%). However, most importantly those females with ST-segment elevation and reversible perfusion defects on stress MPI are as likely if not more likely to undergo left heart catheterization than males; and these females are also as likely if not more likely to have significant flow limiting coronary lesions amenable to intervention or surgery.

7.51

Incremental prognostic value of exercise capacity in risk stratification of patients with left bundle branch block using ECG-gated Tc-99m sestamibi stress myocardial perfusion imaging.

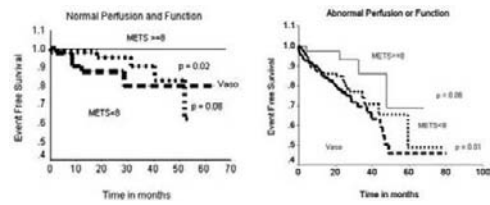
S. Sachin Navare¹, A. Ahlberg², G. Cyr², D. Katten², A. Auser², G. Heller.² ¹Hartford Hospital, Hartford, CT, United States, ²Hartford Hospital, Nuclear Cardiology, Hartford, CT, United States

Background: Pharmacologic stress myocardial perfusion imaging (MPI) is preferred over exercise stress MPI for the diagnosis of coronary artery disease in patients with LBBB. However, there are no data comparing the two modalities for evaluating prognosis.

Methods: We identified 459 consecutive patients with preexisting LBBB who underwent either exercise stress ($n = 240$) or pharmacologic stress ($n = 219$) MPI based on their ability to exercise. Using a 17 segment model and a 5-point scoring system, perfusion was classified as normal (summed stress score [SSS] ≥ 3) and abnormal (SSS < 3) and LV function was classified as normal ($\geq 50\%$) or impaired (<50%). Functional capacity, measured in metabolic equivalents (METS), was determined for patients undergoing exercise stress. Follow-up was complete in 92% of patients (mean 27.5 months).

Results: On follow up, cardiac event (myocardial infarction, cardiac death, unstable angina and revascularization) rates were similar in the exercise and pharmacologic groups (overall: 7.0% vs 7.1%, $p=ns$; with normal perfusion and function: 2.5% vs 6.5%, $p=ns$; and with abnormal perfusion or function: 9.7% vs 13.7%, $p=ns$). However patients whose exercise capacity was > 8 METS had significantly better survival than patients with exercise capacity < 8 METS and those undergoing vasodilator stress with either normal or abnormal perfusion and function. (see picture)

Conclusion: Exercise and pharmacologic stress MPI are equivalent in their ability to risk stratify patients with LBBB. Assessment of functional capacity adds incremental prognostic value over MPI and hence exercise stress MPI should be the preferred modality for risk stratification of patients with LBBB who are able to exercise.



Picture

7.52

ST depression during pharmacological stress testing in patients with left ventricular hypertrophy predicts extensive coronary artery disease.

B. Bruce Darrow, M. Henzlova. Mount Sinai School of Medicine, Medicine/Cardiology, New York, NY, United States

For patients with left ventricular hypertrophy (LVH), ST depression on ECG during exercise stress testing has reduced specificity for the detection of coronary artery disease (CAD). We hypothesize that during stress testing with coronary vasodilators, ST depression is a significant indicator of CAD even if LVH is present.

Methods: We identified 161 patients with suspected CAD who had ≥ 1.0 mm ST depression during adenosine or dipyridamole infusion for stress tests performed between January 1, 2000 and December 31, 2003. SPECT imaging was performed in 114 patients (112 Tc-99m and 2 Tl-201) and PET imaging (Rb-82) in 47 patients. Using standard ECG criteria, 40 patients had LVH (Group 1, LVH+/ST+) and 121 patients did not (Group 2, LVH-/ST+). Patients were excluded for significant LV outflow obstruction, digoxin use, LBBB, paced rhythm, or pre-excitation. A control group included all patients with suspected CAD who had LVH but no ST depression during pharmacological stress (Group 3, LVH+/ST-, n=482). We recorded the incidence of perfusion defects as well as results of 136 patients who underwent subsequent coronary angiography (mean follow-up time 836 ± 29 days).

Results: The groups did not differ in age or gender. As shown in Table 1, the LVH+/ST+ and LVH-/ST+ groups had significantly higher rates of perfusion defects than LVH+/ST- patients. Among those subsequently catheterized, the incidence of CAD (stenosis $\geq 50\%$), as well as multivessel and/or left main disease, was also significantly increased in both the LVH+/ST+ and LVH-/ST+ groups. Similar results were observed when only catheterization data from patients with perfusion defects were analyzed.

Conclusions: ST depression during pharmacological testing is a predictor of extensive CAD not only for patients without LVH but also for patients with LVH on rest ECG.

Table 1.

	LVH+/ST+ Group 1 n=40	LVH-/ST+ Group 2 n=121	LVH+/ST- Group 3 n=482	p (Group 1 vs 3)	p (Group 1 vs 2)
Any perfusion defect	28 (70%)	87 (72%)	204 (42%)	0.0007	NS
Any reversible defect	26 (64%)	83 (69%)	145 (30%)	<0.0001	NS
Multivessel defects	13 (33%)	37 (31%)	62 (13%)	0.0007	NS
Coronary angiography performed (n=136)	13 (32%)	40 (33%)	83 (17%)	0.02	NS
Angiographic CAD	12/13 (92%)	37/40 (93%)	37/83 (45%)	0.001	NS
Multivessel and/or left main CAD	9/13 (69%)	33/40 (83%)	21/83 (25%)	0.001	NS

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Risk assessment with MPI prior to non-cardiac surgery: A real world experience.

G.S. Gregory Thomas¹, T.K. Ip², R.C. Thompson³, D.B. Kramer⁴, D.L. Rice⁵, J.J. Thomas⁶, M.I. Miyamoto⁷. ¹Mission Internal Medical Group, Mission Viejo, CA, United States, ²Mission Internal Medical Group, Mission Viejo, CA, United States, ³Cardiovascular Consultants, Kansas City, MO, United States, ⁴Harvard Medical School, Boston, MA, United States, ⁵Mission Internal Medical Group, Mission Viejo, CA, United States, ⁶Yale University, New Haven, CT, United States, ⁷University of California, San Diego, CA, United States

Background: ACC/AHA guidelines support the role of stress myocardial perfusion imaging (MPI), prior to specific non-cardiac operations in patients with major and intermediate risk predictors. Scant literature exists, however, as to the current clinical use of MPI prior to non-cardiac surgery.

Methods: A prospective evaluation of 5458 patients undergoing stress MPI in a community based outpatient US laboratory.

Results: MPI was performed prior to non-cardiac surgery in 291 patients (5.3%, "Preop") vs. the remainder ("Nonop"). Preop patients were older, 67.9 ± 11.9 yrs vs. 64.6 ± 16.8 ($p < .004$) and more frequently underwent adenosine stress, 70% vs. 38% ($p < .0001$). Exercise stress was performed in 26% and 60% and dobutamine in 4% and 3% of the Preop vs. Nonop groups, respectively. Preop and Nonop groups did not differ according to gender (41% women vs. 35% $p = NS$) or post-stress EF (59.8% vs. 59.2%). Table 1 describes the type of non-cardiac surgery performed.

Conclusion: While substantial evidence supports the use of MPI prior to vascular surgery, MPI is much more commonly used prior to other operations, most notably orthopedic, representing 48% of the population, and prior to a relatively new procedure, gastric bypass (6%). These findings suggest the need for studies of the relative utility of MPI prior to these procedures. While MPI is not expected to be indicated prior to low risk surgery, these patients represented 6% of the population.

Types of non-cardiac surgery

HIGH RISK	
Aortic & major vascular	5%
INTERMEDIATE RISK	
Carotid	1%
Head & Neck	2%
Abdomen & chest (gastric bypass in 6%)	22%
Orthopedic	48%
Prostate & Bladder	5%
LOW RISK	
Endoscopic & superficial	1%
Eye	4%
Breast	1%

Stratified by ACC/AHA cardiac risk category

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Left ventricular dysfunction after vasodilator stress is more accurate than perfusion for diagnosis of coronary artery disease.

RS. Regina Druz¹, K.J. Nichols², O.O. Akinboboye¹, N. Reichek¹. ¹St. Francis Hospital, Cardiac Imaging Research Group, Roslyn, NY, United States, ²Long Island Jewish Medical Center, Department of Nuclear Medicine, New Hyde Park, NY, United States

Background: Three-vessel coronary disease (3VD) is difficult to detect by perfusion imaging due to balanced ischemia. We hypothesized that post-stress left ventricular (LV) dysfunction should more accurately identify 3VD.

Methods: 86 pts. (74 ± 12 yrs; 58 male) with rest Tl-201/adenosine Tc-99m sestamibi scans were identified: 43 with known/suspected coronary stenoses with ≥ 1 segmental reversible defect, and 43 age- and sex-matched controls with no coronary disease and normal LV perfusion and function. Perfusion was based on a 20-segment/5-point summed difference score (SDS), with a cut-off ≥ 8 for extensive defects. Segments with no tracer uptake were excluded to lessen partial volume effects. LV ejection fraction (EF) and end-systolic volume (ESV) were quantified at rest and 60 min post-adenosine by QGS (Cedars-Sinai Medical Center, Los Angeles, CA). LV dysfunction post-adenosine was defined as EF decrease $\geq -12\%$ ($= 2$ SD of the mean EF decrease in controls: $-0.9 \pm 6.0\%$). LV dilation ratio was measured by ESV adenosine: rest. Angiography was performed in 36/43 pts with segmental defects, and 15/36 pts had 3VD. McNemars test ($p < 0.05$) was used to compare $SDS \geq 8$ vs. EF decrease $\geq -12\%$ for tests sensitivity, specificity and accuracy for 3VD.

Results: See Table.

Conclusion: LV dysfunction manifested as stunning, with decrease in LV EF and LV dilation in patients with extensive reversible defects, especially those with angina. A decrease in EF was more specific and accurate for 3VD than perfusion. Thus, gated rest and stress studies had improved diagnostic yield over perfusion for 3VD.

Table

EF decrease $\geq -12\%$	Angina	SDS	ESV adenosine:rest	EF $\geq -12\%$ for 3 VD	SDS ≥ 8 for 3VD
(-); n=33	9%	6+5	1.3+0.2	Sens/Spec 87%/82%*	Sens/Spec 87%/48%
(+); n=10	44%*	10+5*	1.7+0.3*	Accuracy 83%*	Accuracy 62%

* $p < 0.05$

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Prognostic value of heart rate response in patients with atrial fibrillation undergoing gated SPECT Tc-99m sestamibi exercise stress testing.

E. Ernest Podrasky, M. Henzlova. Mount Sinai Medical Center, Cardiology, New York, NY, United States

OBJECTIVE: Pharmacologic control of ventricular rate with anticoagulation is a well-established management strategy for atrial fibrillation (AF). However, the clinical significance of heart rate control during exercise testing is unclear. We sought to determine the prognostic value of heart rate control, with regard to mortality and hospitalization for cardiovascular causes, in patients undergoing exercise stress testing done in conjunction with myocardial perfusion imaging.

METHODS: We reviewed a total of 16,109 consecutive patients who underwent myocardial perfusion imaging between January 2000 and December 2003. Of those, 130 had AF and had undergone exercise testing. A heart rate index (HRI = maximum heart rate/# METS achieved) was calculated for each patient to adjust for level of exercise. Patients were divided into a rate-controlled group ($HRI < 10$; n = 56) and a rate-uncontrolled group ($HRI > 10$; n = 74). Mortality data was obtained from the National Death Index, and hospitalizations were determined by review of hospital records. Presence of CAD and LVEF were assessed by gated SPECT Tc-99m sestamibi myocardial perfusion imaging. Mean follow-up was 29 ± 10 months.

RESULTS: There was no difference between the rate-controlled and uncontrolled groups with respect to age (mean = 70.3 vs. 72.2 years), sex, baseline heart rate (mean = 72 vs. 75), number of medications used (mean = 1.3 vs. 1.2), LVEF (mean = 58% vs. 57%), or presence of CAD (73.2% vs. 64.9%), respectively ($P > 0.05$ for all subgroups). Exercise capacity was significantly greater in the rate-controlled group (mean = 8.3 METS vs. 4.6 METS for the rate-uncontrolled group, $P < 0.00001$). There was 1 death (1.8%) in the rate-controlled group vs. 5 deaths (6.8%) in the rate-uncontrolled group ($P = 0.18$). Twelve patients (21.4%) in the rate-controlled group were hospitalized for cardiovascular causes, vs. 24 patients (32.4%) in the rate-uncontrolled group ($P = 0.12$). For the combined endpoint of death or hospitalization, there were significantly fewer events in the rate-controlled group than in the uncontrolled group (21.4% vs. 37.8%, $P = 0.03$).

CONCLUSION: Heart-rate control during exercise testing is associated with better exercise capacity and improved cardiovascular outcomes in patients with AF. The heart rate index measured during exercise stress testing may be a useful tool for assessing the adequacy of ventricular rate control.

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Incremental prognostic power of adenosine SPECT myocardial perfusion imaging in high risk patients for coronary artery disease: a comparison with cardiac catheterization data.

RT. Robert Tuttle¹, L.S. Linda Shaw¹, MWH. Michael Hanson², S. Salvador Borges-Neto.³ ¹Duke Clinical Research Institute, Medicine, Durham, NC, United States, ²Duke University, Nuclear Medicine Dept., Durham, NC, United States, ³Duke University Medical Center, Radiology/Nuclear Medicine, Durham, NC, United States

Background: Adenosine SPECT myocardial perfusion imaging provides prognostic information in patients with suspected coronary artery disease (CAD); limited data however, are available on the incremental prognostic value of this modality in high risk patients with angiographically documented coronary artery anatomy. Therefore, the purpose of this investigation was 1) to evaluate the prognostic value of adenosine SPECT myocardial perfusion imaging for predicting adverse events in a high risk patient population with coronary angiography and 2) to compare the prognostic value of adenosine SPECT with that of cardiac catheterization data. **Methods:** We studied a total of 662 patients who underwent cardiac catheterization and adenosine SPECT imaging. The mean follow up was 2.3 years for cardiovascular death(CVD). Using Cox proportional hazards regression models, we 1) examined the relationship between adenosine SPECT and CVD after adjusting for a previously-validated baseline clinical index and, 2) compared the prognostic value of adenosine SPECT with that of angiographic data (number of diseased vessels). **Results:** During the follow-up period, 86 patients died from cardiovascular causes. After adjusting for clinical information, adenosine SPECT provided significant incremental prognostic information: incremental Chi-sq = 6.27; p = 0.012 for CVD. Furthermore, adenosine SPECT provided prognostic information above that provided by clinical and cardiac catheterization combined: incremental Chi-sq = 4.5; p = 0.03 for CVD. **Conclusions:** Adenosine SPECT imaging adds significant incremental prognostic information to clinical and cardiac catheterization data for the prediction of cardiovascular death in high-risk patients with angiographically documented CAD. Furthermore, adenosine SPECT imaging can further risk-stratify patients even after considering clinical and cardiac catheterization data.

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The utility of myocardial perfusion imaging and duke treadmill score in predicting outcome in Hispanic versus Caucasian women.

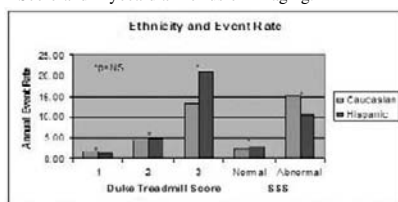
J. Justin Lundbye, S. Werden, F. Kazi, A. Whalen, G.L. Noble, D. Katten, D. O'Sullivan, A. Ahlberg, W.E. Boden, G.V. Heller. Hartford Hospital, Cardiology, Hartford, CT, United States

Background: The utility of SPECT myocardial perfusion imaging (MPI) and Duke Treadmill Score (DTS) has been well characterized in the general population. These testing methods however, have not been evaluated in women of different ethnicities. The purpose of this study was to determine whether DTS and MPI differ in predicting outcome in Caucasian versus Hispanic women.

Methods: Women with intermediate or high pretest likelihood of CAD who underwent ETT/Rest Tc99 Sestamibi MPI (n=1,177) were categorized as low, moderate or high risk DTS. MPI was categorized as normal or abnormal. Mean follow-up was 2.38 ± 1.2 years for all-cause mortality, revascularization (>60 days), and non-fatal myocardial infarction was evaluated by ethnicity.

Results: Caucasian comprised 71.5% and Hispanics 28.5% of the population studied. There were no significant differences between the groups with respect to CAD risk factors. Women with a low risk DTS (≥5) had an overall annual event rate of 1.70% (Caucasian 1.76 %, Hispanic 1.13%, p=0.79). Similarly, moderate and high risk DTS had an annual event rate of 4.38% (White 4.29% Minority 4.83, p=0.74), 13.86% (White 13.15% Minority 21.01%, p=1.0), respectively. A similar observation was seen in Summed Stress Score (SSS). Women with a normal SSS (<4) had an overall annual event rate of 2.39% (White 2.35% Minority 2.44%, p=0.88) while an abnormal SSS (≥4) had an overall annual event rate of 11.76% (White 15.13% Minority 8.40%, p=0.10). (Chart)

Conclusion: Outcome in Hispanics versus Caucasians does not differ when comparing Duke Treadmill Score and Myocardial Perfusion Imaging.



Outcome in Women

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Stress Tc-99m sestamibi ECG-Gated SPECT is effective for risk stratification of patients with left ventricular systolic dysfunction and suspected CAD.

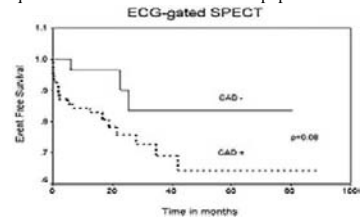
A. Amir Ausef, A. W. Ahlberg, D. O'Sullivan, P.G. Danias, G.I. Papaioannou, I. A. Leka, W. E. Boden, G. V. Heller. Hartford Hospital, Cardiology, Hartford, CT, United States

Background: Stress Tc-99m sestamibi ECG-gated SPECT is highly sensitive for the detection of coronary artery disease (CAD) in patients with left ventricular (LV) systolic dysfunction. However, the value for risk stratification of this population is unknown.

Methods: We identified 164 consecutive patients without known CAD and LV ejection fraction (EF) < 40% (mean 30 + 7) on stress ECG-gated SPECT who underwent cardiac catheterization (CC) within 90 days (mean 12 + 16). Significant CAD by CC was defined as a >50% diameter stenosis. Using a 17-segment model, the following criteria were used for detection of significant CAD by ECG-gated SPECT: summed stress score (SSS) >8 or summed difference score (SDS) >0 or regional wall motion variance (RWMV) >0.114. Patients were followed for myocardial infarction (MI) or cardiac death (CD).

Results: Of the 128 patients who fulfilled criteria for CAD by ECG-gated SPECT, 92 (71.9%) had significant CAD by CC. Conversely, 30 of the 36 (83.3%) patients who did not fulfill criteria for CAD by ECG-gated SPECT did not have significant CAD by CC. Follow-up was complete in 156 (95.1%) patients (mean 33.2 + 24.4 months). Of these, 24 (15.4%) had MI or CD of which 21 (87.5%) fulfilled criteria for CAD by ECG-gated SPECT. Each of the patients with MI (n = 15) had a SSS >8 or SDS >0 (mean 13.8 + 4.8 and 5.3 + 3.9, respectively). Patients with a SSS 8 and SDS = 0 and RWMV <0.114 (CAD-) had better cardiac event-free survival than those with a SSS >8 or SDS >0 or RWMV >0.114 (CAD+).

Conclusion: ECG-gated SPECT is effective in risk stratification of patients with LV systolic dysfunction and suspected CAD. These findings support a role for this noninvasive technique as an initial evaluation in this population.



Kaplan-Meier survival curve

7.59

Prognostic value of myocardial stunning as detected by gated SPECT during a cardiac perfusion stress test.

M. Mario Beretta, S. Viñas, A. Gonzalez, I. Vidal, A. Renner, F. Mut. Asociacion Espanola, Nuclear Medicine, Montevideo, Uruguay

Objective: To investigate if myocardial stunning during a diagnostic stress test, defined as a transient ischemic dysfunction of the left ventricle, has prognostic value in patients with known or suspected coronary artery disease (CAD). **Methods:** A population of 128 patients (pts.) was analyzed (76% men), ages 61 ± 11 years, which were submitted for stress myocardial perfusion studies with 99mTc sestamibi. Fifty pts. had previous myocardial infarction (MI). Stress test was exercise in 94 cases and dipyridamole in 34. A gated SPECT study was performed both in the rest and post-stress periods using a two-day protocol, and left ventricular ejection fraction (LVEF) was calculated for each situation using QGS software. A decrease of at least 10% in post-stress LVEF with respect to the basal (rest) value was considered positive criteria for diagnosis of myocardial stunning. Additional variables included the presence of reversible perfusion defects, a rest LVEF value >40% and ECG changes with ST ≥1.5 mm. Hard (death, MI) and soft (unstable angina, revascularization, cardiac failure, arrhythmia) cardiac events were recorded over a follow-up period of 74 ± 2.7 months. Chi-square test was applied for statistical analysis. **Results:** Stunning was observed in 24% of cases, basal FEVI 40% in 22%, ischemic perfusion pattern (reversible defects) in 52% and ST ≥1.5 mm in 30%. Thirty-five percent of pts. who exercised and 33% of those receiving dipyridamole demonstrated stunning (p=ns). Thirty hard events (26 deaths) and 38 soft events were registered. Myocardial stunning was predictive of total cardiac events (p=0.007) and hard events (p=0.02) but not of soft events (p=ns). Basal LVEF >40% was predictive of total events (p=0.0005) and both hard and soft events separately (p=0.025 and 0.045 respectively) while reversible defects and ST ≥1.5 mm were predictive of total events but not of hard or soft events separately (p=ns). **Conclusion:** Myocardial stunning defined as a negative variation of ≥10% in post-stress LVEF compared with basal LVEF determined by GSPECT can be observed during both exercise or dipyridamole stress tests, and represents a variable of prognostic value in pts. with known or suspected CAD.

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