

## **Clinical Predictors of Abnormal Tl-201 SPECT Myocardial Perfusion Imaging in Elderly Patients Without a Previous History of CAD**

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**Background:** Myocardial perfusion imaging (MPI) has been shown to be of value for the diagnosis of coronary artery disease (CAD) in patients with an intermediate pretest probability of CAD. Although elderly patients are not included in this category, MPI is routinely used in this group. The aim of this study was to identify the clinical predictors of abnormal myocardial perfusion imaging (AMPI) in this group of pts. without a previous history of CAD.

**Methods:** The study population included 339 pts,  $\geq 80$  years old (mean age =  $83.3 \pm 2.7$ ) who were referred to stress Tl-201 SPECT MPI for the diagnosis of CAD.

**Results:** An AMPI was present in 154 pts (45.4%). The incidence of AMPI was significantly higher in males in comparison with females (57% vs 37%,  $p < 0.0003$ ) and in diabetics (57% vs 43%,  $p = 0.038$ ). Anginal syndrome and pulmonary edema were more frequently in those with AMPI than with a normal MPI (49% vs 30%,  $p = 0.0005$ ) and (6% vs 1%,  $p = 0.0072$ ), respectively. In contrast to non-anginal chest pain more frequently reported with normal MPI (30% vs 19%,  $p = 0.016$ ). AMPI was present in 53% of pts with an abnormal resting ECG in contrast to 36% of with a normal ECG ( $p = 0.0017$ ). Based on multivariate analysis the best predictive model of an AMPI (Chi-Square 44.8,  $p < 0.0001$ ) included the following independent variables: male gender, Diabetes, anginal syndrome, pulmonary edema and resting ECG.

**Conclusion:** In very elderly pts without a previous history of CAD, male gender, Diabetes, anginal syndrome, pulmonary edema and resting ECG are clinical predictors of an abnormal MPI.

## Pulse Pressure – A Readily Available Independent Predictor of Extent of Coronary Artery Atheroma on 64 Slice Coronary CT Angiography in Asymptomatic Patients with Type 2 Diabetes Mellitus

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**Background and aims:** Identification of high risk sub-groups for early initiation of preventive medical therapy requires widespread population screening using simple, inexpensive tests. High pulse pressure (PP) has been shown to predict adverse coronary events. We examined the predictive value of PP for the presence of coronary plaque on 64 slice coronary CT angiography (CTA) in asymptomatic pts with type 2 diabetes mellitus (DM) and no history of CAD enrolled in an ongoing prospective outcomes study.

**Methods:** Resting systolic and diastolic blood pressure were measured in both arms, mean pulse pressure calculated and CTA performed in 426 pts (63.5±5.3 yrs, 58% women) with DM (mean duration 10.3±7.8yrs) and no history of CAD.

**Results:** Risk factors included current or past smoking history in 44% and hypertension in 67%. Baseline therapy included insulin in 35%, ACE inhibitor or angiotensin receptor blocker in 67%, calcium channel blocker in 23%, beta blocker in 28% and statins in 70%. Prevalence of single vessel and multivessel plaque and of coronary stenosis in relation to quartiles of pulse pressure are shown in table. Pulse pressure remained a predictor of multivessel coronary plaque after normalization for mean or systolic blood pressure. In a multivariate model including UKPDS risk score (age, gender, duration of diabetes mellitus, blood pressure, smoking history, cholesterol/HDL-C ratio and HBA1C), pulse pressure was an independent correlate of the presence of multivessel coronary plaque (OR 1.17/10mmHg increase in PP, 95% CI 1.01-1.32, p=0.036).

Prevalence of coronary plaque in relation to pulse pressure

Pulse pressure Quartiles (mmHg)	Any plaque N (%) pts	Multivessel plaque N (%) pts	Stenosis (>50%) N (%) pts	Multivessel stenosis N (%)
1 (<49)	73 (69)	44 (42)	19 (18)	6 (6)
2 (49-58)	75(70)	55 (51)	28 (26)	8 (8)
3 (59-66)	82 (81)	62 (61)	23 (23)	5 (5)
4 (>66)	93 (88)	71 (67)	27 (26)	8 (8)
p-value	0.002	0.001	ns	ns

**Conclusions:** In asymptomatic pts with DM and no history of CAD undergoing 64 slice CTA: 1. Pulse pressure predicted the presence and extent of coronary plaque 2. This correlation was independent of mean or systolic blood pressure and independent of the UKPDS risk score. 3. Predictive value of pulse pressure should be further investigated as a readily available screening test for coronary disease in diabetic patients.

## Characteristics of Ischemia and Prediction of Mortality in 1,488 Elderly Women

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The rate of cardiac vascular death is (CD) higher in elderly women than men, although severe CAD is more common in men. Hence it is not really obvious whether detection of severity of ischemia is correlated with CD in women.

**Methods:** During 2005-6 we recruited 1488 consecutive elderly women aged 75 and more (mean  $79 \pm 3.6$  ranges from 75 to 94) who underwent stress MPI. The women were followed for  $29 \pm 18$  months to determine the predictors of CD.

**Results:** There were 160 (11%) total deaths, 114 (8%) of cardiac origin, with annual rate of 3.3%. Reasons for referral were cardiac related symptoms in 77%, history of CAD in 36%, post MI 16%, and post CABG 14% and PCI procedures 24%. Risk factors: diabetes 26%, hypertension 75%, and hyperlipidemia 53%. The majority of women (83%) underwent stress test with dipyridamole and myocardial ischemia was detected in 30%, of them 12% was of moderate to severe.

The univariate predictors of CD were: age, abnormal rest ECG, diabetes, ST depression during stress test, LV enlargement (transient), increased lung uptake, abnormal MPI, ischemia and degree of ischemia. However, the major independent predictors of CD except of age were: LV dilatation (OR 1.7, 95% CI 1.2-2.4,  $p=0.002$ ) and increased lung uptake (OR 2.0, 95% CI 1.1-3.7).

**Conclusion:** The majority of the elderly women referred for MPI cannot perform exercise, and need to be assessed by pharmacological test. The predictors for CD in elderly women are more related to signs of global ischemia rather than regional ischemia.

## **The Predictive Value of Resting Electrocardiogram in Elderly Patients Without a Previous History of CAD for the Diagnosis of CAD by Stress Thallium Myocardial Perfusion Imaging**

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**Background:** Resting electrocardiogram (ECG) has a limited value for the diagnosis of coronary artery disease (CAD). Therefore stress-testing ECG is indicated. Since elderly patients are not able to perform an exercise stress test, are frequently referred to myocardial perfusion imaging (MPI). The aim of the present study was to evaluate the predictive value of resting ECG for the diagnosis of CAD by MPI in elderly pts. without a previous history of CAD.

**Methods:** The study population included 339 pts,  $\geq 80$  years old consecutive who were referred to stress-redistribution Tl-201 SPECT for the diagnosis of CAD.

Based on the resting ECG at time of the MPI study, patients were classified in two groups for comparison.

**Results:** Group A included 182 pts (53.7%) with an abnormal ECG and group B 157 pts (46.3%) with a normal ECG. Group A pts compared with Group B were significantly older ( $82.9 \pm 2.4$  vs  $83.6 \pm 2.6$  years old,  $p < 0.015$ ). More frequently males had an abnormal ECG in comparison with females (70.7% vs 41.7 %,  $p < 0.0001$ ). No significant differences were observed between the groups regarding the prevalence of risk factors and the presence of anginal pain. By visual analysis an abnormal MPI was present in 154 pts (45%). A significant different MPI distribution was observed between the groups, the incidence of abnormal MPI was significant higher in Group A than in B in 97(53.3%) vs 57(36.3%),  $p = 0.0017$ , in addition a normal MPI was present in 100 (63.7%) group B pts.

**Conclusions:** In elderly pts without a previous history of CAD, resting ECG has a significant predictive value for the diagnosis of CAD by Thallium MPI.

## **In Asymptomatic Type 2 Diabetics in Israel do Differences Exist in Effort Tolerance and Prevalence of Coronary Atheroma on 64 Slice Coronary CT Angiography between Patients Living in Town and Country?**

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**Background:** Residual life expectancy of kibbutz members reaching the age of 50 has been shown to exceed that of Israeli town dwellers by >2 years. The study examined whether pts with type 2 diabetes mellitus (DM) living in a rural setting had better exercise tolerance and less coronary artery atheroma than their urban counterparts.

**Methods:** The study examined asymptomatic individuals with DM and no history of coronary artery disease, 55-74 yrs participating in a prospective ongoing outcomes study. Pts underwent symptom limited treadmill exercise stress testing and 64 slice cardiac CT angiography preceded by calcium scoring.

**Results:** Pts in rural areas had less hypertension (53% vs 71%, p=0.002), a shorter history of DM (7.4 vs 10.7 yrs, p<0.001) less were treated with insulin (11.5% vs 31.3%, p=0.001) and HBA1C was lower (6.9% vs 7.7%). Maximal exercise achieved by women in the rural setting was greater than their urban counterparts (8.4 vs 7.3 Mets, p=0.005) and a similar tendency was found in men (10.9 vs 10.1Mets, p=0.08). Independent predictors of lower effort tolerance were older age (p=0.001), female gender (p=0.001), longer history of DM (p=0.014) and urban residence (p=0.07). Urban men had higher coronary calcium scores than rural men (p=0.025) but this was not the case among women. The extent of coronary atheroma was similar in both groups. Independent predictors of multivessel atheroma were older age, male gender and duration of DM.

**Conclusions:** 1. Multiple differences were found between baseline characteristics of rural and urban asymptomatic pts with type 2 DM. 2. Amongst women rural residence was an independent predictor of greater exercise capacity. 3. A similar extent of coronary atheroma was found in both cohorts although the calcified component of atheroma appeared to be greater in urban than rural men.

## Israel Multicenter Perfusion Imaging Survey (IMPIS) 2007: Final Overall Results

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**Background:** Myocardial perfusion imaging (MPI) plays an important role in the non-invasive diagnosis of coronary artery disease (CAD) and pts risk stratification. Although guidelines recommendations and regulations have been published for the use of this diagnostic modality, significant differences through the world have been reported. The main purpose of this study was to prospectively collect data regarding the practice of nuclear cardiology units in 6 public hospitals in Israel. **Methods:** The study population included all consecutive pts who were referred for a MPI, to each of the hospitals during 1 calendar month (02/07). Overall data and percentage centers range data are presented.

**Results:** Within this period 1325 pts underwent a MPI study, 18% (3-41%) of them were hospitalized. The overall clinical characteristics of the pts were: mean age  $65.5 \pm 12$  years old, 59% were males, with known CAD in 45%, angina syndrome was present in 51%, shortness of breath in 17% and 26% were asymptomatic. The stress protocols used were: Dipyridamole in 56% (42-59%), exercise in 41% (34-58%) and dobutamine in 1%. Gated acquisition was done in 45%(0-69%). MIBI was used in 41%(0-85%) and Thallium in 59%(15-100%). Normal MPI was observed in 48% (27-56%).

**Conclusion:** The overall findings of this multicenter survey reflect the wide heterogeneity in clinical practice. The different stress protocols used and the MPI results may reflect the different referral populations to each center.

## **Israel Multicenter Perfusion Imaging Survey (IMPIS) 2007 Comparison between Hospitalized and Ambulatory Patients**

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Myocardial Perfusion Imaging (MPI) is widely used in the evaluation of coronary artery disease (CAD). Until now, there has been no multicenter data concerning the routine practice of nuclear cardiology in Israel.

**Methods:** A multicenter survey was performed during 1 month (February 2007). We prospectively reviewed all consecutive patients (pts) who had undergone MPI in the departments of nuclear cardiology in 6 public medical centers (Asaf Harofe, Beilinson, Ichilow, Hasharon, Kaplan and Soroka).

**Results:** Of 1316 MPI, 240 (18.3%) were performed in hospitalized pts. We found no differences between ambulatory and hospitalized pts in demographics or risk factors, except for a higher proportion of smokers (25% vs 16%,  $p=0.001$ ) in hospitalized pts. Also the hospitalized pts were more likely to have a history of myocardial infarction (34% vs 24%,  $p=0.002$ ) or PCI (33% vs 26%,  $p=0.003$ ) and were less proportion of asymptomatic pts before the MPI (9% vs 22%,  $p<0.001$ ), than ambulatory pts. Despite these differences, we found a similar percentage of pts with normal (49% vs 48%) and ischemic (37% vs 40%) MPI, but more hospitalized pts had fixed defects (30% vs 23%,  $p=0.03$ ) in the MPI.

**Conclusions:** In this first multicenter registry of MPI in Israel, 18.3% of the studies were performed in hospitalized pts. They had more frequent history of CAD (myocardial infarction and PCI), and consequently more fixed defects in MPI. Nonetheless, the incidence of normal or ischemic MPI between the groups was similar.

## Israel Myocardial Perfusion Imaging Survey (IMPIS) 2007. Comparison between Patients with Known and Unknown Ischemic Heart Disease

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There is little information on patients referred for nuclear cardiology studies in Israel. On behalf of the Israel Nuclear Cardiology Working Group we performed in February 2007 a survey of all myocardial perfusion imaging studies (MPI) performed during a period of one month in six major Israeli hospitals. We report about the differences between patients (pts) referred with known ischemic heart disease (IHD) and patients referred to evaluate potential IHD.

During the survey period of one month 1325 patients were studied in the participating hospitals. IHD was known in 569 pts (43%) and 695 pts (57%) were referred due to suspected IHD.

	<b>Known IHD</b>	<b>Unknown IHD</b>
Mean age	67 years	64 years
At least one risk factor	98%	90%
Diabetes Mellitus	40%	28%
Hypertension	76%	65%
Hyperlipidemia	84%	60%
Smokers	19%	16%
Hospitalized pts	18%	15%
Main reason for referral	Assessment of ischemia -72%	Roll out IHD - 81%
Exercise test	37%	45%
Pharmacological stress	63%	55%
Ischemic ECG changes	17%	14%
Abnormal MPI	69%	32%
Ischemic myocardium	53%	28%

Our survey shows that risk factors for IHD are relatively frequent in pts suspected of IHD, who are referred for MPI. The ability of MPI to detect significant ischemia in those pts was high. The results may indicate an under utilization of MPI in searching for significant IHD in pts with multiple risk factors for IHD.

## **Fast Triage of Patients with Acute Pulmonary Embolism by Grading the Reflux of Contrast to the Inferior Vena Cava on CT Pulmonary Angiography**

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**Purpose:** To investigate whether fast grading of contrast reflux to the inferior vena cava (IVC) on CT pulmonary angiography (CTPA) could predict short term mortality in patients with acute pulmonary embolism (PE).

**Methods:** CTPA studies of 135 patients with PE and 123 patients without PE were assessed for: retrograde reflux of contrast to the IVC using visual grading of 1-6 on axial images, pulmonary obstruction index, diameters of pulmonary artery, right and left ventricles. Statistical analysis evaluated these parameters in relation to mortality.

**Results:** Moderate and severe degrees of reflux of contrast to the IVC ( $\geq 4$ ) were found in 25(18.5%) with positive CT and 12(9.8%) individual with a negative CT (P=0.045). Kaplan-Meier survival curves in 30 days, demonstrated for the group of patients with acute PE, a significant reduction in survival only in individuals with moderate or severe reflux of contrast to the IVC ( $\geq 4$ ) compared to lower grades (P = 0.006). On the contrary, there was no significant reduction in survival in patients with a severe reflux ( $\geq 4$ ) and no PE on CT (P=0.65). Pulmonary obstruction index, diameter of right and left ventricles, their ratio, and pulmonary artery diameter, did not show a statistically significant correlation with survival in patients with and without PE.

**Conclusions:** Moderate or severe degrees of reflux of contrast to the IVC during CTPA is a predictor of early mortality in patients with acute PE. Fast grading of reflux of contrast from the original axial CTPA images may be helpful for immediate patients' triage.

## High Adenine Diet Induces a Reversible Inflammatory Process of Aortic Valve Calcification in Rats

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**Objectives:** Developing an animal model and exploring the pathophysiology of aortic valve calcification (AVC).

**Background:** AVC which is a major hallmark of aortic stenosis can result from renal failure (RF). A diet containing high levels of Adenine has been shown to induce RF and therefore might induce AVC.

**Methods:** 23 rats fed with adenine diet for 7 weeks followed by a normal diet for two additional weeks (diet group), were compared with 10 control rats. Renal function, PTH levels, echocardiography and multislice computed tomography (MSCT) were performed. Eight diet group's rats were further followed in order to assess the reversibility of AVC.

**Results:** After 4 weeks, all diet group rats developed RF with secondary hyperparathyroidism (PTH  $2330 \pm 40$  pg/mL versus  $281 \pm 53$  pg/ml, in controls,  $p < 0.01$ ). At 9 weeks, RF resolved with improvement in hyperparathyroidism state. Echocardiography demonstrated valve calcifications in diet group rats, calcium score by MSCT was significantly higher in the diet group as compared with the controls ( $145 \pm 30$  versus 0;  $p < 0.01$ ). Von-Kossa stain in diet group valves revealed calcium deposits with positive staining for osteopontin (osteoblast marker), and CD68 (macrophage). PCR revealed over expression of osteoblast's specific genes and NF $\kappa$ B superfamily members. Serial MSCT scans revealed significant reduction in AVC after diet cessation.

**Conclusions:** We developed a unique, diet-induced model for AVC that can easily be quantifiable using MSCT. We showed that the process is reversible, involves macrophage accumulation and osteoblast transformation. This model may serve as an important tool in the study of AVC.