DETECTION OF MYOCARDIAL VIABILITY:
NEW APPROACHES

171 | Significance of distal reversibility In infarct territory as determined by SPECT thallium-201: a sign of collateral flow with occluded infarct-related coronary artery

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Background: Following myocardial infarction, the assessment of the presence of flow within the infarct region may be of importance for therapeutic management and prognosis.

Our hypothesis: The finding of combined proximal fixed defect and distal reversibility of thallium-201 (Tl-201) uptake within the myocardial infarction (MI) territory is related to collateral flow supplying the territory distal to the occlusion of the infarct-related artery. In order to test the hypothesis, we performed stress-redistribution SPECT Tl-201 studies in 69 consecutive patients following MI with completely occluded (85 patients) or critically stenosed MI-related coronary arteries (4 patients) at coronary angiography.

Results: Twenty-nine patients (Group A) demonstrated a reversible defect in the distal portion of the MI territory combined with fixed proximal defects, and 40 patients (Group B) had only fixed defects in the MI territory. Collateral flow to the infarct-related artery was observed by angiography in 28/29 patients of Group A and in none of Group B: (Sensitivity 98%; Specificity 100%; Accuracy 99%).

Conclusion: The Tl-201 uptake pattern consisting of combined distal reversibility and proximal fixed defect in myocardial infarction territory is a very accurate sign of collateral flow in patients with totally occluded or critically stenosed infarct-related artery.

172 | Thallium-201 intracoronary injection: an ideal technique for the evaluation of myocardial viability

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Low 201-Tl uptake (3-5% of the dose) and heart to background (HBK) ratio do not allow an optimal myocardial imaging after i.v. injection. Moreover patient total body irradiation is quite high. Method: In order to optimize myocardial viability detection, we performed an intracoronary injection of 6-10 MBq of 201-Tl (IC-Tl) during a diagnostic angiographic procedure in 15 male patients (pts) (mean age 65 ± 6 years). The radiocompound was delivered in 3-4 minutes into the left main (8 pts), right coronary (4 pts) or both vessels (3 pts). All pts were also evaluated 7-14 days later after i.v. injection of 201-Tl at rest or after redistribution imaging. Furthermore at the end of both scintigraphic procedures we obtained a blood and 24 hours urine samples for the evaluation of circulating and urinary activity. Results: we did not observe any adverse event after IC-Tl injection. Quality of intracoronary images was excellent in all cases, with a HBK ratio of 7.3 ± 1.5 vs a HBK ratio of 1.5 ± 0.2 after 201-Tl i.v. administration (p < 0.001). Infero-posterolateral H/BK ratio was particularly more favourable (7.1 ± 1.4 vs 1.3 ± 0.1; p < 0.001), since there was no significant splancinic activity when IC-Tl route was performed. In 1 patient myocardial uptake was detected in an akinetic segment with IC-Tl, but not with i.v. injection. In all the other pts 201-Tl uptake did not show any difference between the two studies. Serum and 24 hours urine radioactivity was, by far, lower with IC-Tl route (23 ± 15 vs 292 ± 35 Bq/ml; p < 0.001 and 165 ± 25 vs 2231 ± 57 Bq/ml; p < 0.001). Conclusion: these preliminary data demonstrate the feasibility of IC-Tl injection, that can be safely and easily performed at the end of a routine diagnostic angiographic procedure. For the optimal image quality, the reduction of total body irradiation and the limitation of cost, this procedure could be ideal for detecting hibernated myocardial segments in selected pts undergoing coronary angiography.

173 | Rest-redistribution thallium SPECT versus FDG SPECT to predict functional recovery after revascularization

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In this study we compared rest-redistribution thallium SPECT (RR) with FDG SPECT to predict functional recovery after revascularization. Contractile function was evaluated before and 3 months after revascularization with echocardiography, using a 13-segment model and a 4-grade scoring system. Twenty-four patients underwent RR and FDG SPECT on the same day. The early thallium image obtained in the RR protocol served also as a perfusion study for the comparison with metabolic Imaging. The SPECT data were analyzed semi-quantitatively, employing circumferential profiles and a polar map display. The polar maps were aligned to the echocardiographic segmental model. On thallium/FDG SPECT, dysymetric segments were classified as viable if normal perfusion or increased FDG uptake in perfusion defects (mismatch) was present. For RR, criteria for viability were both the percentage of thallium uptake and reversibility as defined by ROC analysis. Adequate revascularization was accomplished in 106 of the 113 dysymetric segments. Improvement of function was observed in 36 segments.

174 | Myocardial structure correlates with thallium uptake but not with recovery of ventricular function in patients with hibernating myocardium

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The term hibernation describes a state of chronic myocardial dysfunction, reversible after reperfusion. The morphological correlates of hibernation have been investigated in 23 patients with poor left ventricular function and severe coronary disease on angiography who underwent coronary artery bypass graft surgery. The patients were assessed pre-operatively by thallium rest redistribution scanning and magnetic resonance imaging (MRI). And their myocardium was regionally classified as reversibly ischaemic, infarcted, hibernating, or normally perfused. Per-operative biopsies were taken from each of these regions and processed for histology and transmission electron microscopy. The patients were followed up with repeat angiography, MRI, and thallium scanning after 3 months for confirmation of their original classification. An area was only classified as hibernating if rest redistribution was accompanied by reversibility on MRI.

Histological examination of the biopsies (n = 51) revealed myocyte hypertrophy and vacuolation, and variable degrees of replacement of myocytes by fibrous tissue (myocyte volume 98-111%). Electron microscopy showed these vacuolated cells to have a reduced myofibrillar content, glycogen accumulation, numerous small mitochondria, and irregularities in the nuclear membrane, as described in previous reports. The frequency with which these cells occurred in the four tissue groups was assessed by semi-quantitative scoring. Variance analysis of this data showed no significant differences between groups (Kruskal-Wallis test h = 4.399, h > 7.815 for 95% confidence). The total myocyte content per unit volume in the biopsies was quantified using formal morphometric analysis of histological sections. Tissue from normally perfused areas had a myocyte content of 66.8 ± 11.2% (mean ± SD n = 13) reflecting the overall poor ventricular function in the patients. Similar myocyte volumes were found in the tissues with high thallium counts classified as hibernating (71.95 ± 17.9% (mean ± SD n = 17)), and as reversibly ischaemic (72.9 ± 7.0% (mean ± SD n = 11; p = NS)). However the Infarcted regions with low thallium counts had a statistically significant decreased myocyte content of 42.7 ± 33.1% (mean ± SD n = 12; p = NS).

In conclusion, the myocyte content correlated well with pre-operative thallium uptake, but the degree of cell loss and the changes in individual cells were equivalent in both hibernating and non-hibernating tissue. This suggests that these cellular features are not uniquely characteristic of hibernating tissue.
Glucose uptake in the myocardium with changes in coronary flow and glucose concentration – theoretical basis of postmortem emission tomography 'mismatch' concept

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Hypothesis: Positron emission tomography (PET) records a mismatch in "hibernating" myocardium whereby a decreased coronary flow is accompanied by increased glucose uptake. This finding is contrary to well-established dogma from the isolated rat heart that glycolysis is inhibited in ischemia. We therefore examined the relationship between glucose uptake and increased glucose concentration, to determine the kinetics of glucose uptake at a range of low coronary flows including very low values.

Methods: The isolated Langendorff perfused rat heart was perfused under standard conditions for 15 min, followed by flow rates of 0.1, 0.2 or 0.5 ml/g wet wt/min for 30 min. Glycolytic flux was assessed using 2-[3H]-glucose. Glucose concentrations of 0, 2.75, 5.5, 11 or 22 mM were used throughout.

Results: Mean glucose uptake over 30 min plotted against glucose concentration was described by a rectangular hyperbola for each flow rate (control (15 ml/min) y = 1.8/(5.0 + x), 0.5 ml/min y = 1.9/(3.2 + x); 0.2 ml/min y = 1.4/(4.6 + x); 0.1 ml/min y = 0.5/(1.3 + x)), with the maximum rate of uptake dependent on coronary flow. When glucose uptake was expressed as % extraction ( = [glucose uptake / (glucose concentration · coronary flow)]100) and plotted against coronary flow for each glucose concentration, a negative exponential relationship was seen ([11 mM y = 28.69 exp(-0.20) + 5.75 exp(-2.54)]. A significant increase in % extraction was seen as flow rates fell below an extrapolated value of 1 ml/g wet wt/min.

Discussion: Glucose uptake at each flow rate followed Michaelis-Menten kinetics. Under low flow conditions in the isolated rat heart, glucose uptake was increased relative to glucose availability, with increased extraction. At no flow rate did glucose extraction decrease, as would have been expected if glycolysis were inhibited. These results substantiate previously unaccountable findings of "mismatch" between coronary flow and glucose uptake in underperfused tissue.

Identification of viable myocardium by FDG postmortem emission tomography in patients with diabetes mellitus using euglycemic hyperinsulinaemic glucose clamp

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The insulin clamp method has been shown to improve FDG uptake in diabetic patients. To compare the predictive accuracy of NH3/FGD PET imaging under euglycemic hyperinsulinaemic glucose clamp (EHGC) in diabetic and non diabetic pts, we studied 53 coronary pts with anterior wall dysfunction before coronary revascularization. Ten of those pts had diabetes mellitus (8 non insulin dependent, 2 insulin dependent), while the remaining 43 pts had normal fasting glucose. Recovery of ejection fraction by echocardiography 6 months after revascularization. Wall motion improved in 35 pts after revascularization, who were considered to have viable myocardium, while it remained unchanged in the remaining 18 pts. During EHGC, diabetic pts needed less infusion of glucose than non diabetic pts to stabilize glycaemia (0.16 ± 0.05 vs 0.20 ± 0.15 g/min, p < 0.05). Absolute FDG uptake in remote regions was similar in diabetic and non diabetic pts (44 ± 14 VS. 44 ± 17 µmol/min/100 g). Relative anterior FDG uptake in dysfunctional viable myocardium was similar in diabetic and non diabetic pts (70 ± 21 vs 67 ± 15%, p = ns). With univariate analysis, presence of viable myocardium was significantly associated with absolute anterior blood flow (F = 5.3), relative anterior FDG uptake (F = 4.9) and the presence of a mismatch pattern (F = 4.2). None of these parameters were influenced by the presence or absence of diabetes. The predictive accuracy of the presence or absence of a NH3/2-DG mismatch pattern for detection viability was similar in diabetic and non diabetic pts (7/10 [70%] vs 29/43 [67%, p = ns]. Thus, with euglycemic hyperinsulinaemic glucose clamp, the return of contractile function following revascularization can be predicted with the same accuracy in diabetic and non diabetic pts.

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PATHOPHYSIOLOGY OF MYOCARDIAL ISCHAEMIA: NEW MECHANISMS

A genetic risk factor of myocardial infarction identified as a determinant of coronary artery vasoinhibition

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From epidemiological and experimental evidence the components of the renin angiotensin-system are highly suspected to play a role in the occurrence of acute coronary events. Recently, two genetic polymorphisms of the genes encoding angiotensin converting enzyme (ACE) and angiotensin II type 1 (AT1) receptor have been implicated, through a synergistic effect, in the occurrence of myocardial infarction. In this study, subjects bearing the ACE deletion (D) allele and homozygous for the AT1 receptor C1166 transversion allele were at high risk of myocardial infarction.

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To assess the influence of the ACE and AT1 receptor gene polymorphisms on coronary vasomoritlty, we studied in vivo the response of human coronary arteries after intravenous injection of insulin or a patient-specific agonist. A consecutive series of 140 patients with normal coronary arteries, vasomoritlty parameters were estimated with the use of quantitative coronary angioigraphy. No affect of the ACE gene polymorphism could be detected. However, the patients carrying the AT1 receptor CC genotype had a significantly higher vasodilatation of distal coronary artery segments compared to patients with AA or AC genotype (23 ± 5% vs 11 ± 2% or 21 ± 2%, respectively, p < 0.009).

This study demonstrates that the AT1 receptor genotype directly influences coronary vasomorition in humans.

Increased muscular anaerobic glycolysis associated with insulin resistance in patients with angina and normal coronary arteries (syndrome X)

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Patients (pts) with syndrome X (SX) have been suggested to be insulin resistant. The aim of the present study was to assess the effects of suvrametabolical insulin levels on forearm glucose uptake (FGU) and forearm intermediate metabolite balance (forearm lactate and alanine release – FLR-FAR – and forearm pyruvate uptake – FPU) in 8 pts with SX (6 females, 52 ± 3 years, BMI 24.4 ± 0.8 kg/m2) and in 6 control subjects (C) (4 females, 45 ± 3 years, BMI 23.2 ± 0.8 kg/m2). An insulin bolus (0.1 U/kg) was administered in all subjects and blood glucose levels were maintained at basal values by means of a variable rate glucose (20%) infusion. FGU and lactate, pyruvate and alanine balance were measured during the following 60 min. Blood glucose was successfully clamped with a coefficient of variation below 8%. Forearm blood flow was similar in both groups. Basal glucose, insulin, FGU and forearm intermediate metabolites were similar in the two groups. FGU increased in both groups and radioactivity peak at 15 min (3.2 ± 0.8 vs 5 ± 0.7 U/m100 ml/min, p < 0.01). Intermediate areas of FLR were 3.8 ± 6.3 U/m100 ml/min per 60 min in SX pts whilst decreased slightly in C. No differences were found in FPU. The incremental area of FGU was significantly greater in C than in SX pts (183.2 ± 21.7 vs 100.2 ± 20 U/m100 ml/min per 60 min, p < 0.01). The incremental areas of FLR were 3.8 ± 6.3 U/m100 ml/min per 60 min, in SX pts (p < 0.01) and −12.8 ± 6.9 U/m100 ml/min per 60 min in C (p = 0.06). A positive correlation between FGU and FLR was found in SX pts (r = 0.70; p < 0.05) while the reverse applied in C (r = −0.75; p < 0.03). In conclusion, at suvrametabolical insulin levels, SX pts show a decrease in insulin-mediated FGU suggesting the presence of a reduced response to insulin associated with increased anaerobic glycolysis. Primary metabolic abnormalities may therefore play a role in this syndrome.