Results: The percentage of CD4+ was stable over time. The percentage was significantly increased in 
STEMI (6.2, 5.4-6.7) vs controls (5.4, 4.6-6.2), vs 
CSA (3.5, 4.5-6.4) and vs nSTEMI (4.7, 4.4-5.7), while in nSTEMI a 
not significant trend (P = 0.08) towards a overall reduction in CD4 number was observed. The 
expression of CD69 was higher in STEM1 (1.0, 0.7-1.5) vs nSTEMI (0.5, 0.7-1.4), 
P = 0.05. A significantly increased expression of HLA-DR in nSTEMI (9.2, 5.2-18.1) 
was observed vs controls (2.0, 4.4-5.1, P = 0.01) and vs 
CSA (3.2, 1.5-6.8, P = 0.001). The balance between 
activation and regulation, expressed as the ratio of Treg and activation markers was 
altered in CAD groups showing an increased activation of T-cell response. Moreover a 
decreased CCR5 Treg expression was observed in STEM1 (20.7, 13.5-32.8) vs 
controls (31.3, 23.3-39.2, P < 0.05). These data seem to indicate a decreased 
tussial migration ability since CCR5 represents a chemokine receptor for Treg 
homeing. We observed a 2-fold increase in IL-10 levels in STEM1 (4.1 pg/ml, 2.4-14.7) vs 
controls (2.0 pg/ml, 1.6-2.2) and vs nSTEMI (2.0 pg/ml, 1.7-2.9), 
both P < 0.01. IL-6 showed an increased serum concentration both in nSTEMI 
(6.9, 4.5-16.5) and STEM1 (6.7, 4.2-24.9) vs controls (3.1, 2.3-4.5), P < 0.001 
for all. IL-10/IL-6 ratio, used to determine the cytokine suppression/activation 
balance, was decreased in nSTEMI (0.7, 0.3-1.0) vs controls (0.6, 0.4-1.2), 
vs CSA (0.5, 0.3-0.8) and vs STEM1 (0.7, 0.3-1.0), P < 0.001 for all. 

Conclusion: This study showed a pro-inflammatory imbalance both in T-cell 
response and in cytokine network in all CAD groups as compared to controls. 
These findings could help understanding a possible detrimental role of Treg 
in patients with various manifestations of coronary artery diseases. The 
variability we observed so far may reflect the complexity of the pro- 
and anti-inflammatory network which still needs to be explored further.

7. EXPANSION OF T-CELL RECEPTOR e2m EFFECfOR T CELLS IN ACUTE CORONARY SYNDROMES

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Background: Expansion of 
the T-cell receptor (TCR)-e2m family is a main sensor and 
regulator of lymphocyte responses. Loss of TCR-e2m expression has been 
documented during infectious and inflammatory diseases and determines 
a reorientation of effector T-cell (TCR+) trafficking to affected tissues.

We assessed the expression and functional correlates of circulating TCR-e2m 
cells in coronary artery disease.

Methods and Results: We examined the expression of TCR-e2m by flow 
cytometry in 140 subjects. Increased peripheral blood CD4+ TCR-e2m 
cells were found in patients with acute coronary syndromes (ACS), 
mean median 5.3%, inter-quartile 2.4-9.1% of total CD4+ T cells. P < 0.001) compared to 
chronic stable angina (CSA, n = 32); 1.8% (1.0-4.1%) and controls (n = 42), 
1.5%; 0.3-2.9%). Such increase was significantly greater in ACS patients 
with elevated levels of C-reactive protein (CRP > 2 mg/l; 7.7, 3.8-11.3, P < 0.04) 
compared to patients with ACS and low CRP levels (<2 mg/l; 3.3, 1.7-7.7, 
N = 25), P < 0.003, and it persisted after the acute event. Moreover, TCR-e2m 
cells were also more represented in ACS compared to CSA and controls 
within CDB T cell subset (4.0, 2.5-7% vs 1.2, 0.8%-1.6% 0.6-2.9%; 
P < 0.001), NK subset (3.1, 2.4-7.5% vs 1.8, 0.5-7% vs 0.3, 1.3-8.3%; 
P < 0.001 and CD4+ CO2R+ subset 67.5; 52.3-92.9% vs 3.6, 1.5-20.9, 
11.9-13.31, P < 0.001). Finally, CD4+ and CD8+ T cells isolated 
from ACS displayed an augmented transendothelial migratory capacity.

Conclusions: TCR-e2m cells, an effector T-cell subset with trans-endothelial 
migratory ability, are increased in ACS, and may be implicated in coronary 
instability.

8. THE METABOLIC SYNDROME DOES NOT ADD TO CARDIO ARTERIOSCLEROSIS BEYOND WHAT IS EXPECTED BY RISK FACTOR COUNTING OR RISK SCORING

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Objective: The aim of this study was to assess if the Metabolic Syndrome (MS) 
has any add-on effect on subclinical atherosclerosis beyond that expected 
by risk factors (RF) counting or risk scoring.

Methods: Intima-media thickness (IMT) of carotid arteries was assessed by 
using B-mode ultrasound in 1805 patients (56-13 y; 52% women) attending a 
cardiovascular prevention program. Patients with (cases) or without (controls) 
MS according to NCEP ATP III criteria were 1:1 matched for sex, age 
and either the number of conventional RF (Analysis 1) or the Framingham risk 
score (Analysis 2). IMT was assessed in 775 patients from more than 3 components 
of the MS were accepted as RF in the control group.

Results: Cases:control matches were 211 for Analysis 1 and 244 for Analysis 2. 
In both analyses, the number of significant findings was greater in patients with 
positive IMT and carotid IMTmax was found between cases and controls in both analyses (Analysis 1: IMTmax 1.03±0.28 vs 0.77±0.17, P<0.001; 
IMTmax 1.90±0.96 vs 1.59±0.92, cases and controls, respectively; p<0.1).

Conclusions: According to our results the metabolic syndrome does not add to 
the extent of carotid subclinical atherosclerosis beyond that expected by RF
CIRCULATORY RISK IN CHILDREN: APOLIPOPROTEIN A-I AND NON-HDL-CHOLESTEROL

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Objective: Atherosclerosis starts in childhood although clinical manifestations of cardiovascular disease (CVD) do not usually emerge before the middle age. Clinical studies have established that elevated cholesterol (TC) and triglycerides (TG) levels, low high density lipoprotein-cholesterol (HDL-C) and raised lipoprotein(a) (Lp[a]) levels are associated with increased CVD risk. Measurements of TC, LDL-cholesterol (LDL-C) and HDL-C are widely recommended for CVD risk assessment. However many studies in adults have demonstrated that apolipoprotein B (apoB) and apolipoprotein A-I (apoA-I) and their ratio have a greater prognostic value than LDL-C. Furthermore, it is increasingly being recognized that the non-HDL-C level is a simple and accurate index of CVD risk. Aim of the study was the evaluation of the TC, LDL-C, apoB and apoA-I levels, apoB/apoA-I ratio and non-HDL-C in a cohort of children affected by primary dyslipidaemia, divided in two groups according to the family history of CVD.

Methods: we studied 285 children aged 10.04±3.34 years (89 FH, 88 FCH, 54 dominant hypercholesterolemia, 40 hypertriglyceridaemia), 11 familial hypercholesterolaemia, 11 familial hypertriglyceridaemia, with a family history of dyslipidaemia and/or premature cardiovascular disease and 74 controls (age 9.35±4.71 years). TC, HDL-C, TG, apob and apoa-I were measured by an enzyme immunoassay. LDL-C was estimated using Friedewald formula while non-HDL-C was calculated as TC minus HDL-C. Patients were divided in two groups according to a positive (group 1) or negative (group 2) family history of CVD.

Results: dyslipidemic children showed TC, LDL-C, apoB, apoB/apoA-I ratio and non-HDL-C levels significantly higher (p<0.001) than controls. We found significant differences in HDL-C and apoA-I ratio levels comparing the two groups of patients, however they only approached the statistical significance level (p=0.0383 and p=0.06 respectively). Any difference of TC, LDL-C and apoA-I was detected.

Conclusion: The present findings indicate the prognostic value of childhood apoB/apoA-I ratio and non-HDL-C levels in evaluating CVD risk. Measurement of apolipoproteins (apoB and possibly apoA-I) should be routinely added to the standard lipid profile (TC, TG, HDL-C) to assess the atherogenic potential of inflammatory factors relevant to dyslipidemias characterized by an elevation in plasma triglycerides. The apoB/apoA-I ratio and non-HDL-C represent an advantage over traditional lipid variables for risk prediction and especially apoB could also replace the standard lipid profile "as a target for therapy in at-risk patients."

IMPACT OF PERIPHERAL GIRELIN ADMINISTRATION ON BODY WEIGHT, ADIPOKINE PROFILE AND LIVER FAT IN HIGH-FAT DIET OBES RATS

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Rationale: Girelina is a gastric orexigenic hormone whose plasma concentration declines in obesity, with an emerging role in the modulation of insulin action, mitochondrial-lipid metabolism and inflammation. Obesity is commonly characterized by hepatic triglyceride accumulation that can further reduce liver and body insulin sensitivity and is associated with cardiovascular disease. The potential metabolic impact of girelina administration in obesity models is unknown.

Methods: In a rodent model of high-fat diet induced obesity (DIO: Wistar male 3-month-old rats fed 25% fat diet for one month) we measured the effects of 4-day twice-daily subcutaneous girelina injection at a non-orexigenic dose (200 µg/injection; G) on: (a) food intake, total body weight and selected visceral and subcutaneous fat pads; (b) plasma hormonal-metabolic profile [insulin, ghrelin, free fatty acids (FFA), adipokines]; (c) hepatic mitochondrial oxidative capacity (citrate synthase enzyme activity), activated (phosphorylated) master regulator of lipid oxidative metabolism AMP-activated protein kinase (AMPK) and triglyceride content.

Results: Compared to control animals fed a standard diet, DIO gained -10% excess body weight with heavier (P<0.05) visceral (epididymal and retroperitoneal) fat pads. Plasma free fatty acids and leptin/adiponectin ratio was higher (P=0.05) while no significant difference was observed in plasma glucose and insulin. Liver triglyceride content was higher in DIO in spite of comparable tissue mitochondrial enzyme activities and higher AMPK phosphorylation (all P<0.05). In spite of superimposable cumulative food intake, G led to higher 4-day body weight gain compared to DIO (14±2 vs 7±3 gms; P=0.05). Visceral fat pads were however comparable while subcutaneous interscapular fat was heavier in G, associated with lower plasma leptin/adiponectin ratio (all P<0.05 vs DIO). Plasma FFA were also lower in G than DIO (P=0.05 vs DIO and control), in the absence of changes in plasma glucose and insulin. Compared to DIO, G did not change liver mitochondrial enzyme activities and AMPK phosphorylation but it resulted in lower tissue triglyceride content, (all P<0.05 vs DIO).

Conclusions: 4-day girelina administration at a non-orexigenic dose is associated with favorable metabolic changes in diet-induced obese animals. In particular, in spite of higher weight gain girelina is associated with potential preferential subcutaneous fat accumulation, lower leptin/adiponectin ratio and lower plasma FFA. These changes might contribute to reduce liver triglyceride accumulation, in the absence of changes in mitochondrial enzyme activities and AMPK activation. The data provide a rationale for further investigation of girelina as a potential treatment for DIO-associated fatty liver.

ETZEIMBE/SIMVASTATIN COMPARED WITH DOUBLING THE DOSE OF SIMVASTATIN IN HIGH CV RISK DIABETICS NOT AT LDL-C TARGET WITH SIMVASTATIN ALONE. A DOUBLE-BLIND, RANDOMIZED ITALIAN STUDY

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Objectives: to compare the efficacy and safety of ezetimibe (EZE) co-administered with ongoing simvastatin (SIMV) vs doubling the dose of SIMV in low-density lipoprotein cholesterol (LDL-C) for 12 weeks of treatment in patients with type-2 diabetes melitus (T2DM), primary hypercholesterolemia and coronary heart disease (CHD). Design: multicenter, randomized, double-blind, double dummy study.

Participants: Twenty-three Italian centers participated in the study. Ninety-three adult subjects with T2DM and CHD, on a stable daily dose of SIMV, were enrolled for at least 6 weeks, with no significant changes in diet and physical activity (FFM 22.6±5.5 kg, BMI 31.1±5.0 kg/m²). EZE (10 mg) or SIMV 10 mg+ezetimibe (EZE/SIMV 10 mg/day) or ezetimibe 10 mg placebo + simvastatin 20 mg (SIMV 40 mg/day) for 12 weeks were included in the experimental treatment group. Outcomes: the primary outcome was the mean percent change from baseline (randomization visit) to endpoint after 6 weeks in LDL-C concentration; secondary outcomes included the: percentage of subjects who achieved the LDL-C goal as defined by the NCEP ATPIII guidelines (+<2.6 mmol/L; <100 mg/dL) in 6 weeks, the mean percent change from baseline in total cholesterol (TC), high density lipoprotein cholesterol (HDLC) and triglycerides (TG) concentrations, the evaluation of safety and tolerability. Results: Eighty-seven subjects (37 in the EZE/SIMV and 50 in the SIMV group) were included in the ITT analysis. EZE/SIMV 10 mg/20 mg produced a significantly greater mean percent change from treated baseline compared with SIMV 40 mg in LDL-C (-12.23% vs -20.82%; p=0.01) and in TC (-20.6% vs -13.25%; p=0.01). A greater proportion of patients (close to statistical significance) achieved an LDL-C goal <2.6 mmol/L with EZE/SIMV 10 mg/20 mg than with SIMV 40 mg (78.4% vs 60.8% [OR=2.81; p=0.05]). There was no statistically significant difference between treatment groups in the percent change of HDL-C (0.85% vs 0.80% in the EZE/SIMV and in the SIMV group respectively) and TG (-8.5% vs -1.8% in the EZE/SIMV and in the SIMV group respectively). The treatment with EZE/SIMV 10 mg/20 mg was generally well tolerated with an overall safety profile similar to that of SIMV 40 mg.

Conclusions: In high-risk subjects with T2DM and CHD not at the recommended ATP III LDL-C target with simvastatin 20 mg, switching to the combination of simvastatin with ezetimibe (inhibiting both the synthesis and the intestinal absorption of cholesterol) produces a greater reduction of LDL-C and gets a greater proportion of subjects to an LDL-C concentration <2.6 mmol/L after 6 weeks of treatment.

VASCULAR AND METABOLIC ACUTE EFFECTS OF ROSUVASTATIN COMPARED TO SIMVASTATIN IN UNTREATED TYLIDINIC DIABETIC PATIENTS

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The effects of statins on glucose metabolism are controversial. In particular, it is not clear if statins may affect insulin sensitivity decreases LDL-cholesterol and vascular reactive improvement in diabetic patients. The present randomized, double-blind trial has been direct to evaluate the acute effects of rosuvastatin compared to simvastatin on glucose control, insulin-sensitivity and endothelial function in diabetic patients with untreated dyslipidemia. Insulin sensitivity non obese male subjects (aged 42±8, mean±SD) with type-2 diabetes in OMD treatment and dyslipidemia were given rosuvastatin 20 mg (Group B, n=10) or simvastatin 20 mg (Group S, n=10 daily) for one week. Blood samples were assessed at baseline and one-week follow-up (differences in mean values assessed by t-test for paired data); BMI, waist circumference, fasting glucose, HbA1c, lipid profile, hs CRP, fibrinogen, leptin, adiponectin, insulin sensitivity assessed by euglycemic-hyperinsulinemic clamp and endothelial function evaluated by brachial artery reactivity technique (BART). At baseline, subjects in the two arms had comparable anthropometric parameters (Table 1). In good glycemic control, fasting glucose 139±24 mg/dl, HbA1c 6.4±0.6% Group S: fasting glucose