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Differentiation of probucol, AGI-1067 seems to be less selective for ABCA1 pathway as it also inhibits ABCG1-mediated cholesterol efflux.

**3** ARTERIAL STIFFNESS IN OBSESE PATIENTS WITHOUT CARDIOVASCULAR RISK FACTORS

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Despite relationship between obesity and cardiovascular disease are widely defined, mechanisms underlying vascular damage in obesity are less clear. In particular it is debated if weight gain might represent an independent condition able to predict atherosclerosis and clinical event or if other conditions could play a significant role. To further fulfill in this topic, in this study we analyzed arterial stiffness parameters, as early marker of vascular damage, in a group of obese patients without cardiovascular risk factors. For this reason we selected a group of 12 non-smoking obese patients (BMI > 30 kg/m²), without cardiovascular disease, hypertension, diabetes or glucose intolerance (fasting glycemia <110 mg/dl) or dyslipidemias. Inclusion criteria was also the presence of renal or liver disease, neoplasms or other conditions or drugs known to affect lipid metabolism. As controls we selected a group of 12 non-obese healthy subjects with the same inclusion and exclusion criteria. In all subjects a fasting blood sample has been drawn for plasma lipid analysis and the analysis of arterial pulse wave has been done by applanation tonometry (SphygmoCor SP'T-301), which is a non-invasive bedside technology able to determine the Augmentation Index (AI) and the velocity (PWV) of pulse wave. We found that obese subjects were significantly older and had systolic and diastolic blood pressure, total, LDL and non-HDL cholesterol levels higher and HDL-cholesterol levels lower than controls. No significant difference was found for AI or PWV between obese patients and controls and no correlation was found between BMI and AI or PWV in all subjects. However AI was significantly positively correlated with age, triglyceride and total, LDL and HDL-cholesterol levels, whereas PWV was positively correlated with diastolic blood pressure and negatively with HDL cholesterol levels. In conclusion our study has preliminary demonstrated that obese patients without cardiovascular risk factors have some significant abnormality of arterial stiffness. These data, wherever further confirmed, reinforce the importance of early preventive tools, before the development of cardiovascular risk factors associated to obesity.

**4** CHRONIC USE OF LIGHT OR REGULAR CIGARETTES AND FLOW MEASURED DILATATION

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Objective: To compare the effect of "light" and "regular" cigarettes on brachial artery (BA) flow mediated dilatation (FMD).

Methods: BA-FMD was evaluated in 45 light-cigarette consumers, in 45 regular-cigarette consumers and in 45 never-smokers. The groups were matched for age, sex and status of hypercholesterolemia. FMD was calculated either considering the percent change of BA versus the "at-rest" diameter or considering the percent change versus the BA diameter measured in the last 60 seconds of cuff inflation (FMDlast-60's). Cigarettes were defined as "light" or "regular" according to the concomitant presence of tar and nicotine amount above or below 9 and 0.8 mg, respectively.

Results: In never-smokers, BA diameter increased during cuff inflation (change: 0.004±0.012; p=0.023). In smokers no changes in BA diameter during cuff inflation were observed (change: -0.001±0.014; p=0.6).

In smokers, FMD was lower than in never smokers both considering the FMDat-rest: (3.4±3.06 vs. 6.3±3.26; p=0.001) and the FMDlast-60's (3.5±3.4 vs. 5.2±3.33 respectively; p=0.007). In the whole group, both FMDat-rest and FMDlast-60's were inversely associated with pack-years (both p<0.001). FMDat-rest of both light (2.78±3.13%) or regular (4.03±1.93%) cigarette consumers were reduced with respect to...
Cytokine and Receptor Pattern of Activated Versus Regulatory T Cells in Coronary artery Diseases


Background: Regulatory T lymphocytes (Treg) play a key role in maintaining self tolerance and in suppression of pathological immune response. In atherosclerosis an imbalance between activated and regulatory T-cell activity might play a role in the development, evolution and instability of plaques. In murine models a reduction in Treg results in increased atherogenesis. Aims of the study: The aim of the study is to evaluate the balance between circulating activated and regulatory T cells in various manifestations of coronary artery diseases (CAD) and the receptor patterns of these cells. The cytokine profile in its activation (IL-6) and regulation (IL-10) balance as expressed by changes in IL-6 and IL-10 was also evaluated.

Materials and Methods: Treg percentage, identified by CD3+CD4+dimCD25+high panel within the CD3+CD4+ T-cell compartment, was assessed in the study by means of 4- and 5-colour flow cytometry with conjugate antibodies (CD3, CD4, CD25, CD69 and CCR5 the 5-colour panel; CD3, CD4, CCR5 and HLA-DR for the 4-colour panel). Circulating levels of cytokines were assessed by the CBA-Flow technology. We studied four groups of patients: 49 healthy controls with no evidence of coronary disease, 36 patients with Chronic Stable Angina (CSA), 34 patients with Unstable Angina/Non ST Elevation Myocardial Infarction (NSTEMI) and 29 patients with ST Elevation Myocardial Infarction (STEMI). The state of activation of CD4+ T cells was determined by measuring two independent markers: CD25, a marker of early activation, and HLA-DR, a marker of late activation. The reactivity of the Treg percentage was assessed by two different measurements at 1 and 3 months in patients and controls, respectively. All values are expressed as medians (25%-75% iq).

Results: The percentage of Treg was stable over time. Treg percentage was significantly increased in STEMI (6.2, 5.4-6.7%) vs controls (5.4, 4.6-6.2%), vs CSA (3.3, 4.5-6.4) and vs NSTEMI (4.7, 4.4-5.3); while in NSTEMI a not significant trend towards a overall reduction was observed. The expression of CD69 was higher in STEMI (1.0, 0.7-1.6x) vs NSTEMI (0.5, 0.7-1.4), p < 0.05. A significantly increased expression of HLA-DR in NSTEMI (2.5, 2.2-3.2) was observed vs controls (2.4, 1.4-2.0) and vs CSA (3.3, 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 STEMI (20.7, 13.5-32.8) vs controls (31.3, 21.3-39.2), p < 0.05. These data seem to indicate a decreased tissue migration ability since CCR5 represents a chemokine receptor for Treg homing. We observed a 2-fold increase in IL-10 levels in STEMI (4.1 pg/ml, 2.4-17.2) vs controls (2.0 pg/ml, 1.6-2.2) and vs NSTEMI (2.0 pg/ml, 1.7-2.9), both p < 0.001. IL-6 showed an increased serum concentration both in NSTEMI (6.9, 4.5-16.5) and STEMI (6.7, 4.2-24.9) vs controls (3.1, 2.5-4.5), 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 STEMI (0.7, 0.3-1.0), p < 0.001 for all.

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

Cytokine and Chemokine Differentiation Pattern in Patients with ST-Elevation Myocardial Infarction (STEMI) Associated with High Levels of Circulating IL-6. Eighteen Cytokines/Chemokines were Assessed Simultaneously with the Flex-Set Capture bead assay (CBA)

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Background: Preliminary analysis of the population enrolled in the Italian, case-controlled First Acute Myocardial Infarction (FAMI) study showed a 3-fold increase in circulating IL-6 in STEMI patients in comparison to controls.

Objectives: We assessed the possible clustering of patients' behavior by means of multiple biomarkers' measurements. In patients with very high levels or low levels of IL-6.

Materials and Methods: Eighteen cytokines/chemokines (IL-2, IL-4, IL-7, IL-10, IL-10, VEGF, FAS-L, GM-CSF, TNF-α, IFN-γ, IL-8, IP-10, MIP-1α, MIP-1β, MCP-1 and MIG) were analyzed simultaneously with the Flex-Set CBA. Assays were performed on a total of 308 serum samples obtained within 6 hours from the onset of chest pain as follows: 109 patients belonging to the fourth interquartile (IQR) of IL-6 levels (IL6high); STEMI with IL-6 median 17.1 pg/ml, IQR 11.9-29.8 pg/ml; 96 patients belonging to the first IQR of IL-6 levels (IL6low) with STEMI with IL-6 median 3.7; 2.7-4.6 pg/ml and 103 controls (IL-6 median 1.8; 2.5-3.5 pg/ml).

Results: The IL6high STEMI versus IL6low STEMI group showed increased levels of 6 out of 18 analyzed cytokines: IL-10 (5.3 vs 2.4 pg/ml; p < 0.001), IL-8 (10.5 vs 2.7 pg/ml; p < 0.001), MIP-1α (4.4 vs 3.5 pg/ml; p < 0.001), MIP-1β (186 vs 63 pg/ml; p < 0.001), MIP-1α (160 vs 81 pg/ml; p < 0.001), MCP-1 (100 vs 68 pg/ml; p < 0.001). Similar levels of all cytokines were found in IL6low STEMI and controls with the exception of IL-10 (2.4 vs 2.0 pg/ml; p = 0.05) which was increased in IL6low STEMI, and MCP-1 (68 vs 92 pg/ml; p = 0.05) which was decreased in IL6low STEMI. Independent analysis of cytokine distribution, taking into account the 6 cytokines and chemokines which were significantly different and the levels of IL-6 and C-Reactive protein, showed a distinct cytokine pattern in the IL6high and IL6low STEMI groups (p < 0.05).

Conclusions: The multi-cytokine approach allowed us to detect an inflammatory pattern in IL6low STEMI patients, consistent with the hypothesis that some patients with STEMI have a multifaceted inflammatory component identified by high levels of circulating IL-6. This subgroup of patients might benefit by immune-modulating therapy.

The metabolic syndrome does not add to carotid atheroma beyond that expected by risk factors (RF) 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) and IMT measurements were expressed as the mean of 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. The number of patients was different: significant differences were found between cases and controls in both analyses (Analysis 1: IMTmax 0.02±0.08 vs 0.07±0.20; Analysis 2: IMTmax 0.19±0.26 vs 0.19±0.50, cases and significant difference in a partial residual analysis). In the Framingham risk score analysis, Analysis 2 (IMTmax 0.1±0.09 vs 0.13±0.10), 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 counting.