Preprinted from NMCD
Volume 18, Issue 1

ELSEVIER

NMCD

Nutrition, Metabolism & Cardiovascular Diseases

An International Journal on Diabetes, Atherosclerosis and Human Nutrition

ISSN 0939-4753

Official Journal of
- the Italian Society of Diabetology (SID)
- the Italian Society for the Study of Atherosclerosis (SISA)
- the Italian Society of Human Nutrition (SINU)

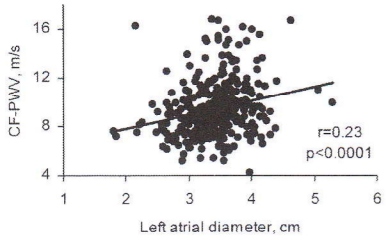
Abstracts of the XXI National Congress of the Italian Society for the Study of Arteriosclerosis (SISA)
21-24 November, Perugia, Italy

that aortic stiffness, an early marker of arteriosclerosis, may be increased in HIV patients not under antiretroviral treatment.
Methods and Results: In 39 untreated HIV-infected patients and 78 age-, sex- and blood pressure-matched HIV-uninfected control subjects, we determined aortic pulse wave velocity by tonometric method. All subjects were free from overt cardiovascular disease and major cardiovascular risk factors. HIV patients had a higher aortic pulse wave velocity (7.5±1.4 *vs* 6.7±1.1 m s^{-1}, p=0.001) than matched control subjects. Age, mean arterial pressure as a measure of distending pressure and HIV infection (all p<0.05) independently predicted aortic pulse wave velocity when a consistent number of cardiovascular risk factors was simultaneously controlled for. Among patients with HIV infection, serum gamma glutamyl transpeptidase concentration was an independent determinant of aortic pulse wave velocity (β=0.46, p=0.003) together with mean arterial pressure (β=0.32, p=0.03).
Conclusions: Aortic stiffness is increased in HIV-infected individuals who have never received antiretroviral therapy. Pulse wave velocity increases with increasing serum gamma glutamyl transpeptidase concentration. We hypothesize that HIV infection is a risk factor for arteriosclerosis.

75 AORTIC STIFFNESS AS AN INDEPENDENT PREDICTOR OF LEFT ATRIAL SIZE IN UNTREATED HYPERTENSION

G. Pucci, G. Schillaci, M.R. Mannarino, J. Helou, V. Giovinazzo, G. Vaudo, E. Mannarino. *Medicina Interna, Angiologia e Malattie da Arteriosclerosi, Università di Perugia*
E-mail: skill@unipg.it

Objective: Left atrial (LA) dimension, a major determinant of atrial fibrillation and cardiovascular outcomes, is primarily dependent on the hypertension-relaated chronic volume and pressure overload. The potential effect of increased aortic stiffness on LA diameter has been understudied in humans.
Methods: 414 consecutive patients with never-treated, uncomplicated essential hypertension, free from diabetes, valvular heart disease and overt cardiovascular disease (age 48±10 years, men 58%, blood pressure 151/94 mmHg), underwent M-mode and Doppler echocardiography, 24-hour blood pressure monitoring and tonometry-based carotid-femoral pulse wave velocity (cf-PWV).
Results: As shown in the figure, cf-PWV had a significant relation to LA diameter (r=0.23, p<0.0001). Patients with LA enlargement (n=37) had higher age-adjusted cf-PWV values than patients with normal LA size (9.89 vs 9.28 m/s, p<0.05). In a multivariate linear regression model, body mass index (β=0.26, p<0.001), body height (β=0.17, p<0.001), left ventricular mass index (β=0.26, p<0.001), and cf-PWV (β=0.18, p<0.001) were all independent predictors of LA diameter, while blood pressure and transmitral Doppler parameters failed to enter the equation.

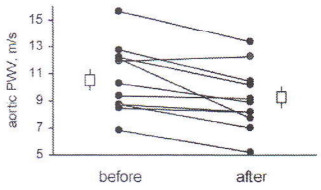


Conclusion: in untreated hypertension, carotid-to-femoral PWV shows a direct association with left atrial size, which is partly independent from the effect of widely accepted determinants of left atrial diameter. We hypothesize that commonly shared pathophysiologic processes, such as chronic inflammation and extracellular matrix remodeling, might underlie this association.

76 AORTIC STIFFNESS: A REVERSIBLE MARKER OF CARDIOVASCULAR RISK IN PRIMARY HYPERPARATHYROIDISM?

G. Pucci, M.R. Mannarino, N. Avenia, M. Monacelli, G. Fabbriciani, M. Pirro, A.M. Scarponi, G. Schillaci, E. Mannarino. *Medicina Interna, Angiologia e Malattie da Arteriosclerosi, Università di Perugia*
E-mail: skill@unipg.it

Background: Patients with primary hyperparathyroidism (PHPT) are at increased risk of death due to cardiovascular disease. Aortic stiffness is an early marker of arteriosclerosis and an important predictor of cardiovascular death. We investigated (Study A) whether aortic stiffness is increased in PHPT, and (Study B) whether parathyroidectomy reduces aortic stiffness over the short term.
Methods and Results: *Study A:* 19 patients with PHPT (age 57±11 years, BP 149/89 mmHg) and 38 age-, sex- and blood pressure-matched control subjects underwent aortic pulse wave velocity (PWV) determination by tonometric method. Aortic PWV was significantly higher among PHTP patients (11.3±2.1 *vs* 9.7±2.4 m×s^{-1}, p<0.01).
Study B: 11 of the PHTP patients were reexamined 4 weeks after surgical parathyroidectomy. As expected, surgery was accompanied by a reduction in serum calcium (from 11.4±1 to 8.9±1 mg/dL, p<0.001) and parathyroid hormone (from 415±472 to 31±27 pg/mL, p<0.001). As displayed in the Figure, aortic PWV decreased after surgery (from 10.6±2 to 9.2±2 m×s^{-1}, p=0.004), and this difference remained highly significant after adjustment for changes in systolic blood pressure.



Conclusions: Primary hyperparathyroidism is associated with increased aortic stiffness compared with normal population. Parathyroidectomy is followed by short-term (4-week) aortic stiffness reduction.

77 UNEXPECTED PITFALLS IN THE MOLECULAR DIAGNOSIS OF HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA

C. Rabacchi[1], M. Ghisellini[1], S. Bertolini[2], S. Calandra[1]. [1] *Dipartimento di Scienze Biomediche, Università di Modena e Reggio Emilia;* [2] *Dipartimento di Medicina Interna, Università di Genova*
E-mail: wavelab@unimore.it

Background: Most patients with the clinical diagnosis of homozygous FH (Ho-FH) carry mutations in the LDL-receptor (LDLR) gene in homozygous/compound heterozygous state. In some patients sequencing results give unexpected results.
Methods And Results. Proband IG, a 30 yrs female with Ho-FH, was homozygous for a mutation in exon 12 (G571E) (FH-Napoli-4) and heterozygous for a mutation in intron 14 (IVS14+5G>A), two mutations previously reported as the cause of FH. The hypercholesterolemic proband's daughter (expected to be obligate heterozygote for G571E mutation) carried the intronic mutation only. This result could be explained in two ways; i) a reversion of G571E mutation to wild type; ii) the presence of a deletion of LDLR involving exon 12, not detected by sequencing. MLPA analysis showed that the proband was heterozygous for a 4kb deletion eliminating exons 11 and 12 and producing a truncated LDLR. This deletion, in linkage with the mutation in intron 14, was regarded as the cause of FH in the daughter. We then asked whether FH heterozygotes carrying the IVS14+5 G>A only, were in fact carriers of the Ex11-Ex-12 deletion. One of these patients was found to be a carrier of a Ex11-Ex-12 deletion, having the same size and break points as those found in proband IG. We also re-examined another patient previously found to be heterozygous for a Ex11-Ex12 deletion (FH-Genova-1), searching for the intron 14 mutation. This patient did not carry the intronic mutation; however, the break points of his deletion were different with respect those of proband IG.
Conclusions. Sequencing results inconsistent with mendelian transmission require further molecular investigations.

78 FAMILIAL AGGREGATION OF CAROTID ARTERY INTIMA MEDIA THICKNESS: A THREE-GENERATION STUDY

A. Ravani[1], M. Amato[1], E. Tremoli[1,2], J.P. Werba[1], D. Baldassarre[1,2]. [1] *Centro Cardiologico "Monzino" IRCCS, Milano, Italia;* [2] *Dept. of Pharmacological Sciences, University of Milan, Italy*
E-mail: alessio.ravani@ccfm.it

Objective: to investigate whether familial aggregation of carotid IMT is influenced by the subjects' age.
Methods: Twenty-four grandchildren (14 men and 10 women), one of their parents (13 men and 11 women) and one of their grandparents (6 men and 18 women), were recruited. Each of them had their CC-IMT_{mean}, Bif-IMT_{mean}, ICA-IMT_{mean} and Mean-IMT measured by B-Mode ultrasound. Simple linear regression analysis by the least squares method was used to investigate correlations between carotid IMT in the *young generational pairs* (grandchildren vs parents) as well as in the *old generational pairs* (parents vs grandparents). For each *generational pairs*, the squared correlation coefficient (r^2) was used to evaluate the extent of offspring's carotid IMT variability explained by the carotid IMT of their respective parents.

Results: The mean age (±SD) of grandparents, parents and grandchildren was 77.3±6.8, 51.5±7.4 and 23.5±7.0, respectively. The corresponding figures for Mean-IMT was 1.45±0.25 mm, 0.94±0.22 mm and 0.63±0.10 mm, respectively. Mean carotid IMT variables of progenitors' correlated with carotid IMT of their offspring in the *young generational pairs* but not in the *old generational pairs*.
Conclusions: Familial aggregation of carotid IMT is better appreciable in the young generational pairs. This may be due to the higher prevalence of potential confounding environmental factors in the older generational pairs.
Funding: Research supported in part by Italian Ministry of Health.

79 INDUCTION OF CXCR2 RECEPTOR BY PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR (PPAR) GAMMA IN HUMAN MACROPHAGES

E. Rigamonti, C. Fontaine, B. Lefebvre, C. Duhem, P. Lefebvre, B. Staels, G. Chinetti-Gbaguidi. *Institut Pasteur de Lille, Lille, France*
E-mail: elena.rigamonti@unimi.it

Objective: Macrophages play a central role in the immune response against infectious organisms. Once activated, macrophages secrete proinflammatory cytokines and chemokines. Interleukin (IL)-8 and related CXC chemokines play a role in the recruitment and activation of phagocytes acting through CXCR1 and CXCR2 receptors. The nuclear receptor Peroxisome Proliferator-Activated Receptor (PPAR)γ exerts anti-inflammatory properties in macrophages, exemplified by the inhibition of cytokine and CC chemokine production. In this study, we investigated whether PPARγ also plays a role in the regulation of the CXC chemokine pathway.
Methods and Results: Surprisingly, we found that synthetic PPARγ ligands increase CXCR2 but not CXCR1 gene expression in primary human macrophages in a PPARγ-dependent manner. The increase of CXCR2 mRNA level was paralleled by an increase in membrane expression of CXCR2 protein as assessed by flow cytometry and western blot analysis. EMSA, ChIP and transient transfection assays indicate that PPARγ activates the CXCR2 promoter by binding to a PPAR Response Element (PPRE). Finally, human macrophages acquire responsiveness to the CXCR2 ligands (IL-8 and Groγ), as measured by analyzing superoxide anion production, following induction of CXCR2 expression by PPARγ ligands.
Conclusions: Our results provide a novel mechanism via which PPARγ can enhance the immune response in human macrophages.

80 BENEFICIAL EFFECTS OF REGULAR MILD PHYSICAL ACTIVITY IN OBESE TYPE 2 DIABETIC PATIENTS

G. Rossi, F. Barone, F. Bellanti, G. Verdile, I. Lagonigro, G. Memoli, M. Rossetti, T. Lo Russo, G. Tanzi, S. Politis, G. Serviddio, E. Altomare. *II Internal Medicine-Department of Medical and Occupational Sciences, University of Foggia*
E-mail: grossi23@alice.it

Introduction: obesity and type-2 diabetes can be considered diseases of physical inactivity. Physical activity is a cornerstone of lifestyle modifications aimed at preventing and managing obesity and type 2 diabetes with related morbidities. The current available epidemiologic evidence supports a substantial benefit from maintaining a physically active, as compared to a sedentary life-style. Clinician counselling and prescription of regular physical activity should represent a major goal in the treatment and primary prevention of obesity and diabetes.
The aim of this study was to investigate the effects of regular mild physical exercise on anthropometric measures, glycaemic and metabolic control in patients affected by obesity and type 2 diabetes but without any pharmacological treatment.
Methods: changes from baseline to 6 months of regular mild physical exercise in total of 40 patients affected by obesity and type 2 diabetes without pharmacological treatment were assessed for waist circumference (WC), body mass index (BMI), fat body mass (FBM), lean body mass (LBM), fasting glycaemia (FG), glycated haemoglobin (HbA1C), total cholesterol (TC), HDL cholesterol (HC), mean arterial pressure (MAP).
Results: significant changes were found for WC (109.95 ± 13.34 cm at baseline vs 103.175 ± 12.56 cm after 6 months, $p < 0.05$), FBM (44.60 ± 6.12% at baseline vs 41.46 ± 6.67% after 6 months, $p < 0.05$), LBM (55.41 ± 6.12% at baseline vs 58.56 ± 6.65% after 6 months, $p < 0.05$), FG (152.65 ± 37.28 mg/dl at baseline vs 123.02 ± 23.37 mg/dl after 6 months, $p < 0.0001$), HbA1C (6.79 ± 1.02% at baseline vs 6.23 ± 0.95% after 6 months, $p < 0.05$), TC (200.81 ± 43.06 mg/dl at baseline vs 174.15 ± 32.47 mg/dl after 6 months, $p < 0.005$), HC (48.55 ± 10.51 mg/dl at baseline vs 54.5 ± 11.1 mg/dl after 6 months, $p < 0.05$) and MAP (109.62 ± 11.85 mmHg at baseline vs 100.62 ± 7.66 cm after 6 months, $p < 0.0005$).
Conclusions: these findings provide some evidence that regular mild physical exercise has beneficial effects on anthropometric parameters, glycaemic and metabolic control in obese type 2 diabetics. Thus, our study suggest that these patients may adopt and maintain a regular physical activity program over 6 months. Future research should utilise larger samples size and longer study durations to confirm this.

81 VASCULAR PREVENTIVE MEASURES: THE PROGRESSION FROM ASYNTHOMATIC TO SYNTHOMATIC ATHEROSCLEROSIS MANAGEMENT. A SYSTEMATIC REVIEW OF EVIDENCE ON EARLY DIAGNOSIS

F. Rubba[1], M. Gentile[2], L. Quagliata[1], M. Triassi[1,2], P. Rubba[2]. [1] *Dott. Economia e Manag. Università Federico II Napoli;* [2] *Dipartimento Medicina Clinica Sperimentale*
E-mail: fabiana.rubba@unina.it

Screening for early-stage asymptomatic cancers to prevent late-stage malignancies has been widely accepted. However, although atherosclerotic cardiovascular disease accounts for more death and disability than all cancers combined, there are no general consensus on prevention measures for asymptomatic atherosclerosis and relative reimbursement.
Data were collected by searching evidence in different databases (PUB MED, Embase, OVID) by using digital libraries networks. Studies published in last ten years were analyzed. 21 studies were included in the review, reporting evidence on early diagnosis.
Variety of screening tests of asymptomatic atherosclerosis are available, and the cost-effectiveness of their use in a comprehensive strategy must be validated. Some of these screening tests, such as carotid artery intima–media thickness (IMT) and plaque by ultrasonography and measurement of coronary artery calcification by computed tomography scanning, have been available longer than others and are capable of providing direct evidence for the presence and extent of atherosclerosis. IMT allow to determinate pre-clinical atherosclerosis and is demonstrated to influence prognosis and global health even in youth and particularly in certain peculiar patient categories as peri-menopausal women. Coronary calcification is a marker of atherosclerosis that can be quantified with the use of cardiac CT and it is proportional to the extent and severity of atherosclerotic disease. The published studies demonstrate a high sensitivity of CACS for the presence of coronary artery disease but a much lower specificity for obstructive CAD depending on the magnitude of the CACS and it remains unclear whether CT screening would provide sufficient extra information over risk factor scoring. Further evaluation and new evidence about the potential role for the emerging biomarkers and imaging techniques could clarify the setting of emerging risk profiles as the metabolic syndrome and help to develop a heightened awareness of patients at risk for future events.

82 RISK MANAGEMENT OF PROGRESSION FROM BRAND TO NON BRAND STATIN FARMACOTHERAPY: LACK OF EVIDENCE AND NEED OF ORGANISATIONAL PATHWAYS OF MONITORING

F. Rubba[1], M. Gentile[2], A. Mattiello[2], L. Quagliata[1], S. Maccarone[1], P. Rubba[2], M. Triassi[1], S. Panico[2]. [1] *Dott. Economia e Manag. Università Federico II Napoli;* [2] *Dipartimento Medicina Clinica Sperimentale*
E-mail: fabiana.rubba@unina.it

EBM based review of clinical and preclinical research on statin therapy demonstrate high prevalence of profit trial conducted by Drug Company, with poor data on effective bioequivalence among statin class. The emergency in drug market of non brand statin molecules seem to suggest the possibility of obtaining a lowering of cost of statin therapy
We conduct a scenario analysis evaluating the potential change of prescription habits with introducing non brand simvastatin and evaluating CVD risk modification calculated by risk chart (http://www.cuore.iss.it/).
The transition to brand simvastatin to non brand simvastatin mean a potential increase of drug adverse reaction (no data of post marketing utilization are now available)
The transition to new generations statins to non brand simvastatin could also produce an amount of people that remain with high cholesterol (pharmacologic activity end-point) and that raise their own cardiovascular risk (with potential effect on efficacy end-points as CV events and mortality); particularly the risk could turn over 20% in diabetic smoking women or diabetic women with high pressure aged between 60 and 69 years with cholesterol over 299 mg/dL, and over 20% in smoking or aged men with similar lipid profiles. More over risk could be high in women aged more than 70 (not included in risk charts).
Despite the reduction of costs connected to less expensive molecules the lack of perception of this transition toward an unfavourable lipid profile could raise the recourse of Hospital specialized facilities with incremental cost of CVD prevention and monitoring (with 2846±872 euro for an average in-patient and 298±77 euro for an average out-patient – Data from Cardiovascular DRG) and could influence the quality of life.