SOCIETÀ ITALIANA PER LO STUDIO DELLA ATEROSCLEROSI (SISA)

Congresso della Sezione Siculo-Calabra

Messina, 9 Ottobre 2017

Nel corso del Congresso Regionale della Sezione Siculo-Calabra della Società Italiana per lo Studio dell'Aterosclerosi (S.I.S.A.), che si è svolto il 9 ottobre 2017 a Messina, sono state affrontate diverse tematiche metaboliche, sia in ambito clinico che genomico/molecolare.

Il primo "hot topic" affrontato è stato il ruolo delle angiopoietine, in particolare dell'angiopoietina tipo 3 (ANGPTL3), nel modulare il metabolismo lipidico; sono stati discussi i trial *clinici concernenti l'inibizione di ANGPTL3 in soggetti ipercolesterolemici, come i pazienti con ipercolesterolemia familiare.*

Il secondo tema discusso è stato il ruolo delle cellule progenitrici dell'endotelio nella patogenesi e nella progressione della malattia cardiovascolare; da diversi studi sperimentali è emerso come la modulazione di tali cellule possa avere importanti risvolti clinici e terapeutici.

Il Congresso ha dato largo spazio ai giovani ricercatori della sezione Siculo-Calabra, che hanno rappresentato il "cuore pulsante" del congresso. In momenti distinti della giornata, i giovani ricercatori hanno presentato i risultati scientifici del loro lavoro più recente, facendo emergere, nel corso della discussione, spunti di riflessione e stimoli di approfondimento per nuovi filoni di ricerca.

COMUNICAZIONI ORALI

EFFETTO DELLA LIPOTOSSICITÀ SULLA TRASLOCAZIONE DEL RECETTORE GABAA IN UNA LINEA DI α CELLULE PANCREATICHE (α-TC1 CLONE 6)

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Razionale. L'acido γ-aminobutirrico (GABA) è il principale neurotrasmettitore inibitorio del sistema nervoso centrale. Questa molecola viene rilasciata contemporaneamente all'insulina dalle β-cellula pancreatiche e contribuisce all' inibisce della secrezione di glucagone nelle alfa cellule pancreatiche.
Scopo dello studio. L'obbiettivo di questo studio è stato quello di analizzare gli effetti del trattamento cronico con palmitato sulla via intracellulare del segnale insulinico, sulla traslocazione del recettore del GABA insulino-indotta e l'effetto del trattamento cronico del GLP-1 sul ripristino di tali vie. Una linea murina di α- cellule pancreatiche, α-TC1 clone 6, è stata esposta cronicamente al palmitato (0,5mM) per 48 ore in presenza o in assenza di GLP-1 (100nM) e successivamente è stata stimolata acutamente con insulina. Alla fine del periodo di esposizione è stata analizzata la concentrazione di glucagone rilasciato nel mezzo di coltura, i livelli di fosforilazione dei componenti chiave del segnale insulinico e la traslocazione del recettore del GABA ($GABA_AR$) sulla membrana plasmatica.
Risultati. Il trattamento cronico con palmitato determinava un incremento della secrezione di glucagone, una riduzione dell'attivazione di IRS1/AKT e della traslocazione del recettore del GABA. Il co-trattamento con GLP-1 induceva il miglioramento dell'insulino-resistenza palmitato indotta, ripristinava la traslocazione del $GABA_AR$) a livello della membrana cellulare e riduceva la secrezione di glucagone.
Conclusioni. Questi dati suggeriscono che il trattamento con GLP-1 potrebbe migliora l'iperglucagomemia associata al diabete mellito di tipo 2.

IL TRATTAMENTO CON N-ACETILCISTEINA È IN GRADO DI PREVENIRE IL DANNO MITOCONDRIALE INDOTTO DALL'ESPOSIZIONE AD ATORVASTATINA IN MODELLI DI β-CELLULE PANCREATICHE

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Razionale. Recenti studi clinici hanno evidenziato un modesto aumento dell'incidenza di diabete mellito di tipo 2 associato all'utilizzo di statine. Tale fenomeno sembra essere legato all'utilizzo di statine di natura lipofilica ed al dosaggio impiegato. Ad oggi, tuttavia, non è chiaro quale sia la causa di questo effetto e quali siano i meccanismi molecolari coinvolti.
Scopo dello studio. Valutare l'effetto di statine di natura lipofilica ed i meccanismi molecolari coinvolti.
Metodi e Risultati. In isole pancreatiche umane ed in cellule beta in coltura continua (INS-1) esposte a diverse concentrazioni di atorvastatina (10 driale generate dal trattamento con atorvastatina.
Conclusioni. Questi dati dimostrano che lo stress ossidativo costituisce un elemento chiave nella patogenesi del diabete indotto dall'uso di statine e pertanto potrebbero consentire di identificare nuove strategie di prevenzione o di intervento per la gestione clinica di pazienti ad elevato rischio di diabete e malattie cardiovascolari.

LOW ADVANCED GLYCATION END PRODUCT DIET IMPROVES THE INFLAMMATORY PROFILEAND ARTERIAL STIFFNESS OF DIABETIC SUBJECTS

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Background. Cardiovascular disease is the leading cause of mortality among individuals with type 2 diabetes, accounting for 40% to 50% of all deaths. One of the most important mechanism linking chronic hyperglycemia with vascular complication is the formation and accumulation of advanced glycation end products (AGEs). B*eside endogenous AGE production*, *AGE*s can also be found in foods and contributes significantly to the individual AGE pool. Modern diets are high in advanced glycation end products (dietary AGEs, dAGEs), derived from processing methods that exert a pivotal role in promoting atherosclerotic risk.
Objective. We studied the effect of low vs standard dAGEs diets (L-dAGEs vs S-dAGEs) on lipid profile, inflammation, and cardiovascular risk in diabetic subjects.
Methods. A 18-week randomized dietary intervention was conducted on 30 diabetic subjects. We evaluated lipid profile, high-sensitivity C-reactive protein, arterial stiffness, and intima-media thickness (IMT).
Results. After 18weeks high-sensitivity C-reactive protein levels were significantly reduced in the L-dAGEs group compared to standard diet (0.32 [0.24-0.38] vs 0.48 [0.38-0.56] mg/dL, P<.05). We observed a non significant reduction in lipid profile in patients with L-dAGEs. With respect to baseline, L-dAGE patients showed a significant reduction in Augmentation index (27±8.6 vs 32.6±5.3%) and Augmentation pressure (21±6 vs 24±7 mmHg). A non significant reduction of Pulse Wave Velocity was observed in L-dAGE group. No difference in IMT was found from baseline to follow-up in both the groups.
Conclusions. L-dAGEs improved the inflammatory profile of diabetic subjects and seemed to reduced arterial stiffness compared with a standard diet. Further studies are needed to recommend this dietary regimen for prevention of cardiovascular risk in diabetes.

HBA_{1C} IDENTIFIES SUBJECTS WITH PREDIABETES AND SUBCLINICAL LEFT VENTRICULAR DIASTOLIC DYSFUNCTION

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Background and Objective. Prediabetes is associated with subclinical cardiac changes associated with heart failure development. We investigated diastolic function and its association with markers of glycation and inflammation related with cardiovascular disease in patients with prediabetes. We focused on individuals with prediabetes identified only by glycated hemoglobin A1c [HbA1c 5.7-6.4% who had normal fasting glucose (NFG) and normal glucose tolerance (NGT) after oral glucose tolerance test (OGTT)].
Main Outcome Measures. HbA1c, OGTT, doppler echocardiography, soluble receptor for advanced glycation end-products (sRAGE), endogenous secretory RAGE (esRAGE) and S100A12 were evaluated in all the participants.
Patients. We recruited 167 subjects with NFG/NGT. Subjects were stratified into two groups according to HbA1c levels: controls (HbA1c <5.7% and NFG/NGT); and HbA1c prediabetes (HbA1c 5.7-6.4% and NFG/NGT).
Results. Patients with HbA1c prediabetes (n=106) showed a lower E/A Ratio compared with controls (n=61) (1.10±0.24 vs 1.18±0.23, $P<0.05$); furthermore, they showed a higher left atrium volume (LAV) (28.4±5 vs 22.1±3, $P<0.05$) and sphericity index (SI) (0.6±0.06 vs 0.5±0.05, $P<0.05$). After multiple regression analysis, HbA1c, and esRAGE were independently associated with E/A Ratio; the major determinants of LAV were HbA1c and sRAGE, whereas SI was associated with HbA1c.
Conclusions. Subjects with HbA1c prediabetes exhibited subclinical cardiac alterations: lower E/A Ratio, higher LAV and impaired SI; sRAGE, esRAGE and HbA1c were associated with these alterations. These subjects would not have been classified as having prediabetes on the basis of fasting glycemia or post-OGTT values.

AN INCREASED WAIST-TO-HIP RATIO IS A KEY DETERMINANT OF ATHEROSCLEROTIC BURDEN IN OVERWEIGHT SUBJECTS

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Aims. The association of overweight status and cardiovascular disease is not clear. In this study we aimed to investigate coronary atherosclerotic disease, evaluated as coronary artery calcium score (CACs), in overweight patients with or without abdominal obesity as defined by waist-to-hip ratio (WHR).
Methods. We enrolled 276 patients aged between 40 and 70 years, with a body mass index of 25-29.9 kg/m^2 and at least one cardiovascular risk factor. Exclusion criteria were history of diabetes, cardiovascular or renal disease. Patients were stratified in high WHR (H-WHR) or low WHR (L-WHR) group according to WHR (≥0.85 for women and ≥0.90 for men) and underwent multi-detector computed tomography for CACs. Mean carotid intima-media thickness (IMT) and plaque presence were equally assessed.
Results and Conclusions. CACs was higher in the H-WHR group compared to L-WHR (9.05 [0.0-83.48] vs 0.0 [0.0-64.7] AU, p<0.01); the prevalence of CACs >0 in the H-WHR group was significantly higher than subjects with L-WHR (59.6% vs 38.5%, p<0.001). Moreover, H-WHR group had higher mean IMT (0.64 [0.56-0.72] vs 0.59 [0.55-0.67] mm, p<0.05) and higher carotid plaque prevalence (63.7% vs 50.8%, p<0.05) compared to subjects with L-WHR. Logistic regression showed that H-WHR was associated with presence of CACs and carotid plaque (p<0.01). In a multiple linear regression, WHR was positively associated with CACs and IMT (p<0.01). H-WHR is a marker of coronary and peripheral atherosclerotic burden in overweight patients.

ANALISI GENETICO-MOLECOLARE IN UNA FAMIGLIA AFFETTA DA IPERTRIGLICERIDEMIA FAMILIARE AUTOSOMICA DOMINANTE

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Background. Hypertriglyceridemia is a common occurrence, whose risk (cardiovascular events, pancreatitis, etc.) increases proportionally with the triglyceride values. It may be secondary to other metabolic disorders or autoimmune diseases or drugs, but the more severe forms generally have a genetic origin and some of these are very rare and difficult to diagnose.
Clinical case. Woman, 48 years, fertile, normal weight (BMI=21), with combined dyslipidemia (mainly hypertriglyceridemia) (total cholesterol 350-480; HDL <30; triglycerides 1300-2500 mg/dL) known for more than 20 years and resistant to diet and n-PUFA 1 g x 4/day (>500 mg/dL). In maternal family, 5/12 uncles had early (50-65 years) cardiovascular events. Her daughter (22 years) has a fenofibrate-resistant hypertriglyceridemia (>1350 mg/dL) and her son (18) has a hypertriglyceridemia (>1500 mg/dL) diagnosed since birth (270-320 mg/dL) but never pharmacologically treated. Both the patient and her children history (glycemia, renal, hepatic and thyroid function, screening for other endocrine and autoimmune diseases, ...) were negative for secondary forms. Our patient had a hepatosteatosis (ultrasonographic diagnosis) but has never had cholelithiasis. A recent Echo-Doppler showed no signs of carotid Intima-Media Thickness. The medical examination did not reveal xanthomas/xantelasms nor discolorations in the skin folds. After 12-hour incubation at 4°C, plasma appeared milky.
Comment. Clinical and laboratory history, together with very high triglyceride levels, resistant to therapy, made us suspect a genetic form.
Diagnosis. Patient's and her childrens' blood samples were sent to the Biomedical Department of Internal Medicine, Palermo University, where they confirmed the diagnosis of hypertriglyceridemia due to heterozygous nonsense mutation (c.718 G>A) in the CREB3L3 gene both in mother and her children.
Conclusions. CREB3L3 hypertriglyceridemia is a very rare form. To date, there are not well defined clinical criteria for diagnosing. Our case, along with very few others already genetically confirmed, could help us in early identifying if there are any common clinical criteria.

DETECTION OF COPY NUMBER VARIATION IN LDLR GENE BY NEXT GENERATION SEQUENCING IN PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA

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Background. Familial Hypercholesterolemia (FH) is a dominant disorder characterized by high plasma LDL-C levels and an increased risk of premature coronary artery disease. It is caused by mutations in three genes: LDLR, APOB and PCSK9. Search for mutations is commonly performed by Sanger sequencing or Next Generation Sequencing (NGS). The majority of LDLR gene variants are point mutations (90-95%) and about 5-10% are due to copy number variations (CNVs) that require further molecular analysis to be characterized (ie Southern Blotting or Multiplex Ligation-dependent Probe Amplification (MLPA). During the last years, NGS based technology has been improved to detect CNVs as an alternative approach. A new bioinformatic tool for Ion Reporter software allow to detect CNVs using NGS data outputs obtained by Personal Genome Machine (PGM).
Objective and Methods. The aim of the study was to test if NGS data could be used to detect CNVs in LDLR gene and validate the results with MLPA. We used an Ampliseq custom panel for the analysis of FH-related genes by Ion Torrent PGM and a bioinformatic tool for the analysis of data to detect CNVs.
Results. The analysis of NGS data outputs of FH patients showed a concordance in LDLR CNVs detection between MLPA and NGS methods. CNVs discovered in FH patients by MLPA were also detected by NGS.
Conclusion. These results indicate that the detection of CNVs by NGS method represent a valid methodology that can reduce cost and time of molecular analysis in FH.

TYPE III HYPERLIPOPROTEINEMIA IN A GROUP OF OUTPATIENTS WITH MIXED HYPERLIPIDEMIA

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Background. Familial dysbetalipoproteinemia(FD) also known as type III hyperlipoproteinemia (OMIM 617347**)** is a genetic disorder of lipoprotein metabolism characterized by mixed hyperlipidemia, remnant accumulation and increased risk for premature cardiovascular disease. FD is an autosomal recessive disease, caused by mutations in the apolipoprotein E gene (APOE). Most familial dysbetalipoproteinemia patients are homozygous for apolipoprotein ε2, which is associated with decreased binding of apolipoprotein E to the LDL receptor. Among people carriers of an ε2ε2 genotype, 15% develops familial dysbetalipoproteinemia, which becomes evident through secondary risk factors, such as obesity and insulin resistance, that facilitate the development of FD by inhibiting remnant clearance and degradating the heparan sulfate proteoglycan receptor.
Objective and methods. The aim of this study was to evaluate the APOE genotype in a cohort of 87 patients presenting with mixed hyperlipidemia at the Lipid Clinic in Palermo. More, among these subjects, we have analyzed those with a prevalent hypertriglyceridemia, transmitted as a dominant trait within a family, to identify the causal mutation of the candidate genes of dominant forms of primary hypertriglyceridemia by direct sequencing. Anthropometric measures, clinical and biochemical parameters, life style (smoker and/or alcohol habits) and cardiovascular outcomes were evaluated.
Results. We have identified the ε2/ε2 genotype in three probands. The phenotypic characterization of these subjects revealed a wide variety in clinical presentation. FD facilitating factors, such as insulin resistance and/or obesity and/or smoking habits conditioned the clinical presentation such as fluctuations of plasmatic triglycerides or the presence of cardiovascular events among siblings. Moreover, the sequencing of CREB3L3 gene led to the discovery of a known missense mutation in one patient with a prevalent phenotype characterized by hypertriglyceridemia.
Conclusions. We identify three patients carriers of ε2/ε2 genotype. The phenotypic expression of FD is greatly affected by clinical and genetic factors.

CHOLESTEROL SYNTHESIS AND GLUTATHIONE METABOLISM GENE PATHWAYS ARE CO-REGULATED IN CONCERT WITH GENES OF UNKNOWN FUNCTIONS. CLUSTER ANALYSIS OF PATTERNS GENERATED FROM A WEB REPOSITORY OF HEPG2 TRANSCRIPTOMES

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Background. Living cells react to external stressors by activating coordinate expression of several genes. Synergism is guaranteed by the coordinating role of transcription factors (TF). The analysis of the whole transcriptome expression by microarray analysis is a valuable tool to discover such patterns of genes co-regulation.
Objective and Methods. This paper analyzed the gene responses of HepG2 cells subjected to various stressors in different microarray transcriptome analyses in order to build patterns of co-regulation and to establish expression correlations between 20382 transcripts and 1896 TF extracted from the same experiments. Microarray transcriptome analyses were retrieved from a web repository and a powerful pipeline was developed to build regulation profiles of transcripts, to cluster them in homogeneous groups and to identify group of clusters sharing similar biological functions.
Results. This approach identified at least four clusters of genes related to: cell cycle and division (area 1), structural constituents of ribosome (area 2), cell division and mitosis (area 3), cholesterol synthesis (area 4). The area 4 contained also transcripts of genes related to glutathione metabolism, energy generation, and four genes of unknown function: *TMEM97, TMEM14A, C14orf1* and *C4orf27*. The correlations of transcripts of cholesterol synthesis with the set of TF showed that some of them emerge as putative regulators of cholesterol metabolism, with *CEBPBP, DDIT3, CDK2* and *FOXM1* as most relevant candidates.
Conclusions. A novel powerful approach for the analysis or co-expressed genes under the control of a series of TF is presented. This approach revealed suggestive links between cholesterol synthesis, transcripts with other functions and TF apparently unrelated at first sight.

PRECLINICAL IMPAIRMENT OF MYOCARDIAL FUNCTION AND ENDOTHELIAL VASCULAR MARKERS IN DRUG-NAÏVE PSORIATIC AND RHEUMATOID ARTHRITIS: ASSOCIATION WITH VITAMIN D LEVELS AND INFLAMMATION

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Background and Aims. Cardiovascular (CV) morbidity is increased in inflammatory joint diseases (IJD), as rheumatoid (RA) and psoriatic arthritis (PsA). Whereas increased prevalence of subclinical atherosclerosis has been reported in these conditions, whether an early myocardial functionality is also impaired remains unknown. The aim of this study was to evaluate the myocardial functionality by speckle-tracking echocardiography (STE) in recent onset RA and PsA patients and its potential associations with the levels of circulating CD34 + cells, vitamin D, and with disease activity.
Methods. STE was used to assess the myocardial functionality in patients with very early RA (n=41) and PsA (n=35) without traditional CV risk factors, and 58 matched healthy controls (HC). Global longitudinal and circumferential strain (GLS and GCS) was estimated. Pulse wave velocity (PWV) and carotid intima-media thickness (cIMT) were measured as surrogate markers of atherosclerosis. Circulating CD34 + counts were evaluated by flow cytometry and vitamin D levels were quantified by HPLC. Disease activity was assessed by Disease Activity Score-28 (DAS28).
Results. RA patients exhibited impaired GLS and GCS (both $p<0.001$) as compared to HC, GLS being also altered in PsA ($p=0.020$ vs. HC). DAS28 was correlated to GLS ($r=0.908$, $p<0.001$) and GCS ($r=0.868$, $p<0.001$) in RA, these findings being confirmed by multivariate regression analyses adjusted for confounders and Principal Component Analyses. GLS and GCS were impaired in PsA patients with high disease activity as compared to HC, and GLS was found to be a predictor of cIMT in this condition. On the other hand, vitamin D was negatively associated with cIMT in HC ($r=-0.308$, $p=0.026$) but not in PsA or RA, although decreased levels were observed (both $p<0.001$). Vitamin D was an independent predictor of decreased CD34 + levels in PsA and RA. CD34 + counts negatively correlated DAS28, GLS and GCS in RA.
Conclusions. Subclinical myocardial dysfunction is observed in IJD patients with preserved left-ventricular function and without traditional CV risk factors. Subclinical myocardial dysfunction was found to be a very early event in IJD. Disease activity was the main predictor of myocardial strain impairment. Interestingly, myocardial function was altered and associated with cIMT also in PsA patients with high disease activity.

A TREATMENT WITH ANTI-PROPROTEIN CONVERTASE SUBTILISIN-KEXIN TYPE 9 MONOCLONAL ANTIBODIES IS EFFECTIVE IN IMPROVING ARTERIAL STIFFNESS BESIDES EXPECTED LIPID PROFILE EFFECTS

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Background. Monoclonal antibodies that inhibit proprotein convertase subtilisin-kexin type 9 (PCSK9) are a new class of drugs able to lower LDL cholesterol levels. This class of drugs is indicated in the treatment of patients affected by familial hypercholesterolemia (FH) and patients affected by acute coronary syndrome (at least six months after the event).
Purpose. We investigate whether after six months of treatment with anti-PCSK9 monoclonal antibodies (alirocumab or evolocumab) may induce any improvement of pro-atherogenic profile and arterial stiffness (AS) in patients with high cardiovascular risk already in treatment with the maximally tolerated statin therapy.
Methods. We enrolled 23 people not at target LDL-C values. At enrollment and 6 months later we evaluated anthropometrics, laboratory profile, pulse wave velocity (PWV) and carotid intima-media thickness (cIMT).
Results. After 6-months of treatment we found a significant decrease of inflammatory markers (hs-CRP: -41.4%; Fibrinogen: -18.8%), LDL-C and lipoprotein(a) levels (respectively -64.2% and -36.2%). PWV (-9.8%) appeared to be improved; cIMT remained unchanged. PWV reduction appeared to be correlated with inflammatory markers and LDL-C reduction. However, ΔPWV appeared to be not dependent on ΔLDL-C or Δfibrinogen by the multiple regression analysis.
Conclusion. After 6 months of treatment the levels of CRP, Fibrinogen, LDL-C, and Lp(a), as well AS indices, are significantly improved as compared to baseline. A treatment with anti-PCSK9 monoclonal antibodies may improve significantly the arterial stiffness in patients with high cardiovascular risk and this result seems to be independent by the improving of lipid profile.

FACTORS ASSOCIATED WITH THE DEGREE OF LIVER AND VASCULAR DISEASE IN PATIENTS WITH NON ALCOHOLIC FATTY LIVER DISEASE: AN OBSERVATIONAL STUDY

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Background and aims. Non-alcoholic fatty liver disease (NAFLD) is defined as accumulation of triglycerides more than 5% in the liver in the absence of other causes of liver disease and with alcohol consumption less than 30 g per day for man and 20 per g day for woman. NAFLD enclose a spectrum of diseases ranging from simply steatosis to end stage liver diseases or to hepatocellular carcinoma (HCC); moreover, people with NAFLD have a higher risk of dying than general population, and the most common causes of death are cardiovascular disease, neoplastic disease and liver disease. NAFLD is becoming a relevant problem because of its high prevalence (~25% worldwide). pathophysiology is not fully understood. The pivotal role of insulin resistance is validated from a huge number of literature, but other factors can take part to liver and cardiovascular damage progression, such as diagnosis of Diabetes Mellitus (DM), Arterial Hypetensions (AH), Dyslipidemia (D), modest alcohol consumption. The aim of this study is to analyze factors associated with liver and cardiovascular damage in patients with NAFLD.
Material and methods. We analyzed the clinical records of 258 patients with ultrasound diagnosis of NAFLD, older than 18 years at the outpatient clinic for the hepatic steatosis of the University of Messina, after the release of informed consent we collected data on anthropometrics data, diagnosis of DM, AH, D. Data on alcohol consumption were collected and patients declaring a consumption lower then the reported cut off were considered as modest consumers of alcohol, whereas the other patients were "not drinkers". Data on liver damage as evaluated by liver stiffness measurement (LSM) were collected. Data on cardiovascular damage evaluated as abnormal cIMT were also collected (only in 133 patients).
Results. LSM indicative of advanced fibrosis correlates with BMI ($p<0.001$), CV ($p<0.001$), Age ($p<0.001$), and is associated with DM ($p<0.001$), AH ($p<0.001$), abnormal cIMT ($p<0.05$). The logistic regression models show that the presence of advanced fibrosis depends on age ($p<0.005$), BMI ($p<0.001$), CV ($p<0.001$), diagnosis of DM ($p<0.001$), AH ($p<0.001$), after adjustment for the other factors BMI and DM are the major risk factors for advanced fibrosis in patients with NAFLD ($p<0.05$, OR 1.188, CI 1.004-1.405; $p<0.05$ OR 3.943, CI 1,221-12,735). The logistic regression models show that abnormalcIMT depends on Age ($p<0.001$), CV ($p<0.05$), DM ($p<0.005$), AH ($p<0.005$), D (0.05), LSM ($p<0.05$). After adjustment for other factors, age results the major risk factor for vascular damage in patients with NAFLD ($p<0.005$).
Conclusion. Our data show no association between modest alcohol consumption and the degree of liver damage. In patients with NAFLD, the presence of type 2 diabetes mellitus and obesity is the main risk factor for advanced liver fibrosis. Since the severity of liver damage is also associated with the presence of vascular damage, it would be useful to suggest this patient to undergo carotid Doppler even to assess global CV risk and personalize the treatment.

NUTRACEUTICAL-POT IN PATIENTS WITH PERIPHERAL ARTERIAL OCCLUSIVE DISEASE AND STATINS INTOLERANCE: MORE THAN A CHANCE

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Aim. Peripheral Arterial Occlusive Disease is a clinical and very common manifestation of atherosclerosis in occidental countries. The main objective of these patients is the reduction of cholesterol levels (LDL-c). This objective improves claudicatio and reduce heart-associated events. We aimed evaluating the efficacy, the safety and the tolerance of a nutraceutical compound in PAOD patients which, due to an intolerance or to a volunteer refuse, weren't in treatment with any statin. We tested the hypothesis of a possible improvement of exercise performances in claudicatio patients intaking an integrator with multiple anti-atherosclerotic principles.
Methods. LDL-c level and treadmill test performance were evaluated on PAOD patients intaking this nutraceutical product were compared to patients in treatment with a placebo at T0 and at T6. The nutraceutical integrator contained: Omega-3: 651 mg; Monascus Purpureus: 417 mg; Policosanol: 10 mg; CoQ10: 10 mg; Resveratrol: 10 mg; Vitamine B6: 3 mg; Vitamine B12: 2.5 mcg, Folic Acid 300 mcg. 68 patients were enrolled and were divided in 2 groups (A group = nutraceutical, B group = placebo). The study had 3 phases: patient selection, screening part and patient evaluation under blind-treatment. Eligible patients had to be older than 40 years and had suffered from claudicatio for more than 6 months.
Results. A Group patients had a progressive and significative reduction of serum levels of total and LDL cholesterol and triglycerides than B group ($p<0,001$). A Group had also better PWV values than control group. Treadmill performance was significantly improved in patients belonging to A group than B group patients.
Conclusions. PAOD patients well tolerated nutraceutical administration and the treatment resulted being secure and effective. Whether it isn't possible using a statin in PAOD patients, a nutraceutical formulation it has to be considered as a valid alternative.

CORRELATION BETWEEN BLOOD LEVELS OF S100B PROTEIN AND INCIDENCE OF HEART FAILURE OR IMA IN A CARDIOLOGY UNIT

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Background. Since the first nineties is has been demonstrated that serum S100B levels were increased in the pathogenesis of heart disease and involved their pathogenetic mechanisms. By the years it was also noticed that after myocardial infarction both mRNA and levels of S100B protein were up-regulated. S100B by interacting with RAGE is able to start an inflammatory response with an increase of adhesion molecules and inflammatory cytokines, leading to another cardiovascular diseases, atherogenesis. On this basis, Cai et Al. investigated whether or not S100B it was a associated with stable angina and acute coronary syndrome obtaining a significant correlation. In fact S100B mRNA levels were increased in large and small infarct areas. Li et Al. dosed S100B serum levels in patients affected by heart failure in order to understand if this protein could be a reliable biomarker in the studied disease. In this study S100B was increased in failing hearts but even more higher in serum of patients that had also chronic kidneys disease. Their work included also the analysis of other disease markers such as hsCRP, TNF-alpha, NT-proBNP levels together with echocardiographic assessment. What emerged was that serum S100B was an independent risk factor for chronic heart failure and for major cardiac events. Data also underlined that higher levels of this alarmin were correlated with a worse prognosis. Differently from the already known heart disease biomarkers, S100B is a tissue-specific protein (chondrocytes, adipocytes, skeletal myofibers, cardiomyocytes, dendritic cells, etc.); it was largely demonstrated to be released after a damage and the consequent remodelling involving cardiac tissue. The obvious consequence is its increase in plasma suggesting S100B to be a more specific marker of heart disease, more than already known biomarkers.
Chronic heart failure is one of the most common consequence of myocardial infarction, and is characterized by a reduction of the heart ability to face peripheral blood distribution. Chronic heart failure (HF) and myocardial infarction (IMA) are often associated to the augmentation of inflammation markers. S100B is an alarmin secreted by damaged cardiomyocites. We examined the correlation between S100B protein serum levels and the incidence of acute heart failure and IMA in symptomatic patients.
Methods. We conducted a prospective study on 90 patients aged between 50 and 72 years accepted to our Unit referring cardiac associated symptoms (thorax pain, dyspnea, arrhythmic symptoms). They were divided in three groups: healthy subjects (group A), chronic heart failure patients (group B) and IMA patients (group C). CRP, NT-proBNP, and routine exam were performed in every patient. Moreover it was made a S100B dosage was made.
Results. Results demonstrated different levels among healthy subjects. However in chronic heart failure patients the alarmin levels were higher but not significantly augmented. Instead AMI patients had mean values of S100B doubled than the other two groups and significantly augmented.
Conclusions. According to our data S100B as the potential to be, in a near future, be considered as an acute myocardial infarction marker in addiction to the ones existing. However more studies are needed to identify possible bias elements in S100B serum dosage. This together with other elements are guiding us to a better understand of micro-structural changes in damaged heart in order to consider new therapeutic targets.