immune complexes with VWF (these complexes are cleared by cells bearing Fc-receptors that bind immunoglobulin G (IgG); b) adsorption of VWF by malignant cell clones; and c) loss of high-molecular-weight (HMW) VWF multimers under conditions of high shear stress. In most instances, AVWS is identified because of bleeding complications: in fact more than 80% of the patients are active bleeders. Recurrent bleeding episodes occur in about 20–33% of patients with AVWS, especially following major trauma and surgery. Because of the heterogeneous mechanisms of AVWS, more than one therapeutic approach is often required to prevent or treat acute bleedings. The treatment goals in AVWS are: to control acute bleeds, to prevent bleeding in high-risk situations, and to obtain long-term remission. Whenever possible, treatment should address the underlying disorder, which can treat the AVWS as well. Patients with AVWS actively bleeding and/or those exposed to major/minor surgery can be managed with desmopressin, VWF/FVIII concentrates, high-dose immunoglobulin, plasma-exchange, recombinant activated factor VII. However, these therapeutic approaches are not always effective in all VWD patients and should be assessed for efficacy and safety by expert hematologists.

Oral communications

Atherosclerosis, diabetes, MS and arterial occlusive diseases I

OC-49
Alcohol consumption and incidence of atrial fibrillation and heart failure: prospective findings from the MOLI-SANI study

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Background: The connection between ethanol and atrial fibrillation (AF) and heart failure (HF) remains controversial. We investigated if categories of alcohol consumption are predictive of onset of AF or HF in the follow up of the MOLI-SANI study.
Methods: We analyzed 22,420 (47% men, age ≥35 years) AF or HF-free individuals randomly recruited from the general population included in the MOLI-SANI study, for whom complete data on HF, AF and alcohol were available. The cohort was followed for a median of 4.2 years (91,930 person-years). Alcohol intake was categorized in former, never, occasional (<1 g/day) drinkers and in four categories of consumers with different intake (Table). Incident cases were identified through linkage to the regional archive of hospital discharges. The end of follow-up was 31/12/2011. Hazard ratios (HRs) were calculated using Coxproportional hazard models.
Results: We identified 546 incident cases of HF and 352 of AF. In comparison with never drinkers, both former or occasional drinkers showed an equal risk of developing HF (Table). Drinking at various amount of alcohol revealed a J-shaped protection against HF, with a 25% (95% CI: 1% to 44%) maximum protection at 2–4 drinks a day, independent from common confounders. Concerning AF, we failed to observe any association of alcohol with onset of it. Very similar results were obtained after restriction of the analyses to only men/women or to type of alcoholic beverages (wine, beer or liquor).
Conclusions: Consumption of alcohol in moderation prevents the incidence of heart failure of 25%, whereas it was not associated with development of atrial fibrillation.

OC-50
Role of NADPH oxidase p22phox gene polymorphisms as determinants of major adverse cardiovascular events in patients with acute coronary syndrome undergoing coronary angioplasty

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Reactive oxygen species (ROS) play a primary role in atherosclerosis. The major source of ROS in artery wall is related to NADPH oxidase activity, where they promote oxidative stress and plaque progression/instability. A higher expression of p22phox protein, a subunit of NADPH oxidase coded by *CYBA* gene, was observed in human atherosclerotic coronary arteries. We evaluated the role of rs4673, rs7195830, rs9932581 *CYBA* polymorphisms on the occurrence of major adverse cardiovascular events (MACE) at 2-year follow-up, in a cohort of n=1361 patients with acute coronary syndrome (ACS) undergoing coronary angioplasty.
The status of A allele carriers (AA+AG) of the rs9932581 polymorphism in the CYBA promoter was associated with MACE protection (59.3% MACE vs. 69.1% noMACE, p=0.03). At the multivariate logistic regression analysis, adjusted for known determinants of MACE, the status of rs9932581 A allele carrier resulted a significant and independent protective factor for MACE (OR=0.634, 95% CI 0.422–0.95, p=0.028). The genotype distribution of rs4673 polymorphism did not show a statistically significant difference between patients with and without MACE, even if the prevalence of T allele carriers (CT+TT) was lower MACE patients. No significant association with MACE occurrence was observed for rs7195830 polymorphism.
Our data suggested that polymorphism rs9932581 in *CYBA* gene plays a crucial role in susceptibility to MACE in high risk vascular patients.

OC-51
Non-alcoholic fatty liver disease and subclinical organ damage: a new predictor of asymptomatic extra coronary atherosclerosis and endothelial dysfunction

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Introduction: We investigated the predictive power of NFLD occurrence in identifying extra-coronary atherosclerosis, evaluated by carotid-IMT (c-IMT) and femoral-IMT (f-IMT), and endothelial dysfunction, in patients with no history of cardiovascular diseases.
Materials and methods: We investigated C-IMT, f-IMT, NFLD, by ultrasound, and endothelial function, by peripheral-arterial-tonometry (PAT), in 125 subjects (M: 71, F: 54; 45.1±15.9 y.o), without history of cardiovascular event, diabetes, liver infection, alcohol consumption, systemic diseases, and the use of drugs causing liver damage. PAT values were expressed as natural logarithm of reactive-hyperemia-index (LnRHI) values, so that <0.4 expressed dysfunction. NFLD was expressed by an eight-point score, so that 0 defined absence and 8 maximum severity of steatosis.
Results: C-IMT >0.9mm was associated to a more marked severity of hepatic steatosis (5.1±2.2 vs 2.4±1.7; p<0.0001) and to a lower endothelial function (0.41±0.07 vs 0.9±0.12; p=0.001); specifically, f-IMT>1.2 mm was associated to higher steatosis score (4.9±2.3 vs 2.5±1.9; p=0.001). ROC for steatosis score showed higher AUC values in discriminating c-IMT>0.9mm (AUC 0.76, 95% CI 0.67–0.84, p<0.0001) and f-IMT>1.2mm (AUC 0.73, 95% CI 0.65–0.81, p=0.0002), compared ROC of cardiovascular risk factors (CRFs), respectively for c-IMT (AUC 0.70, 95% CI 0.62–0.79, p=0.01) and f-IMT (AUC 0.69, 95% CI 0.61–0.77, p=0.027).
Regarding the prediction of endothelial dysfunction, ROC for steatosis score showed higher AUC values in discriminating patients with LnRHI<0.4 (AUC 0.80, 95% CI 0.72–0.87, p<0.0001), in comparison to ROC of CRFs (AUC 0.74, 95% CI 0.65–0.85, p=0.0001).
At univariate analysis, a >3 steatosis score was significantly associated to c-IMT>0.9mm (p<0.0001), f-IMT>1.2mm (p=0.001) and endothelial dysfunction (p>0.0001), even after correction for CRFs at multivariate analyses.
Conclusions: Our study provides evidences that NFLD occurrence and severity may select patients with endothelial dysfunction and extra-coronary atherosclerosis, in a primary prevention population, independently of traditional cardiovascular risk profile. A 3 value of NFLD score may be considered as cut-off of clinical relevance.

OC-52
T-wave axis deviation is associated with inflammatory biomarkers: results from the MOLI-SANI study

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Background: T-wave axis deviation (TDev) is an ECG indicator of ventricular repolarisation and may help identifying subjects at risk for cardiac events and mortality. However, the pathogenesis of TDev is not well established. We aimed at testing a possible low-grade inflammatory origin underlying TDev abnormalities.
Material and methods: Cross-sectional analysis on 17,920 subjects free from major coronary heart and haematological diseases enrolled in the MOLI-SANI study. TDev from a standard 12-lead resting electrocardiogram, was categorized as normal ($\geq$15° to $\leq$75°), borderline (>75° to $\leq$105° or <15° to $\geq$−15°) and abnormal (<−15° to $\geq$ −180° or >105° to $\leq$180°). High sensitivity (Hs) C-reactive protein (CRP), white blood cell (WBC) and platelet counts (PLT), neutrophils (granulocytes) to lymphocytes ratios (GLR) and a novel inflammatory score including all the listed biomarkers were used as markers of inflammation.
Results: Subjects with high CRP levels had 73% and 78% higher odds of having respectively borderline and abnormal TDev in multivariable model; the association was still significant, although reduced, after controlling for body mass index (OR=1.18; 95% CI: 1.05–1.32, for borderline and OR=1.48; 95% CI: 1.06–2.05, for abnormal). GLR and the inflammation score were both associated with increased odds of having abnormal TDev (OR=1.44; 1.14–1.82 and OR=1.57; 1.16–2.11 respectively), whereas no significant relationship was found for WBC or PLT counts. The association between CRP and TDev was significantly stronger in women, younger subjects, not obese individuals, normotensive and in those without metabolic syndrome.
Conclusion: CRP was an independent predictor of abnormal TDev, especially in subjects at low CVD risk. This hypothesis is further confirmed by the association of TDev with other biomarkers of inflammation such as GLR or the novel low-grade inflammation score. These results suggest that a low-grade inflammation likely accounts for the pathogenesis of TDev.
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OC-53
Effect of CHOLACTIV™ supplementation in subjects with moderate cardiovascular risk

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Cholactiv™ is a natural supplement containing lycopene, policosanols from rice, polyphenols and evening primrose oil: the individual components were shown to reduce blood lipid levels, but no reports are available on the effect of their combination.
Aim: To test the efficacy of Cholactiv™ to improve lipid profile and reduce cardiovascular risk in subjects at moderate risk, who do not have indication for statin treatment.
Methods: Placebo-controlled, randomized, double-blind trial with 2 parallel arms. 188 subjects (152 men), 35–69 years, with a global cardiovascular risk between 5 and 19%, received dietary advice plus twice daily one capsule of either Cholactiv™ (n=91) or placebo (N=97) for 6 months. At time 0, after 3 and 6 months, blood and urine were collected for biochemical analyses, blood pressure, pulse rate, height and weight for BMI calculation and waist and hip circumferences were measured; endothelial function evaluated by Endopath 2000, questionnaires for cardiovascular risk factors and dietary habits administered. At 6 months, tests were performed also after a post-prandial oxidative stress.
Results and discussion: Cholactiv™ reduced both total (−8%) and LDL (−5%) cholesterol and triglyceride levels (−18%) after 6-month treatment. The net change on triglyceride and LDL was comparable with that reported after omega 3 supplementation. There was a trend towards a decrease in the global cardiovascular risk, possibly significant with a longer treatment. A significant decrease over time was observed in body weight, BMI and waist circumference both in placebo and Cholactiv™ group; hip circumference decreased only in the Cholactiv™ group. The administration of Cholactiv™ for 6 months was safe, well tolerated and did not induce any relevant side effect.
Conclusion: Cholactiv™, in addition to dietary advice, might produce clinically relevant benefits in the primary prevention of cardiovascular disease.
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OC-54
Prothrombotic propensity of stable angina patients with type-2 diabetes mellitus: focus on platelet-associated tissue factor

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Introduction: Patients with type-2 diabetes mellitus (T2DM) have both a platelet hyper reactivity and a hypercoagulable state. Our group has previously shown that platelet-associated tissue factor (pTF) is increased in coronary artery disease (CAD) patients compared to healthy subjects.
Aim: In this study we assessed whether T2DM affects pTF expression and the overall prothrombotic potential in stable angina (SA) patients.
Methods: We enrolled 30 SA patients with T2DM and 30 without T2DM. pTF was evaluated by flow-cytometry. TF contribution to the prothrombotic potential was analyzed by thrombin generation assay (Thrombinoscope). The global haemostatic function was evaluated by thromboelastometry (Rotem).
Results: T2DM-patients showed significantly higher number of TF^+-platelets compared to no-T2DM patients (30.1±3.6 vs. 13.4±1.7, $p<0.01$) which resulted in an higher platelet-associated thrombin generation, being shorter both the lag-time and the time-to-peak in T2DM patients. Treatment of samples with an anti-TF antibody caused an increased lag-time in both groups, the delay being significantly greater in T2DM-patients. These findings underlie the contribution of pTF to thrombin generation. Similar results were obtained when thrombin generation was assessed in plasma samples. Maximum Clot Firmness, α-Angle and Maximum Velocity of clot formation assessed by ROTEM were all significantly increased in T2DM-patients.
Conclusions: SA patients with T2DM show a higher number of TF^+-platelets compared to no-T2DM patients. pTF is able to trigger thrombin generation, which is blocked by a specific anti-TF antibody. These findings shed new light on the mechanism involved in the enhanced prothrombotic phenotype associated with T2DM.
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Fibrinogen, Factor XIII, and fibrinolysis

OC-55
Oxidative stress and fibrinogen modification in marfan syndrome patients

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Marfan syndrome is a multisystemic, inherited connective tissue disorder with cardiovascular manifestations relevant for the morbidity and mortality of patients. Oxidative stress has been invoked as a pathogenetic mechanism in several human cardiovascular disorders. In particular, our recent study revealed the presence of significantly higher protein carbonyls and, at the same time, significantly lower Total Antioxidant Capacity (TAC) in the plasma of Marfan patients with respect to controls, suggesting the occurrence of systemic oxidative damage in this disorder. Among plasma proteins fibrinogen represents a major target of oxidative modifications.