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(4.4–80.6) vs. 9.5 (0.7–25.5) $\mu\text{mol/L}$; $p < 0.05$) with respect to abstainers and teetotalers, whereas no significant differences for the other parameters investigated have been reported. In order to investigate the relationship between type and amount of alcohol consumption and thrombophilic risk factors we performed a general linear model after adjustment for possible confounders. By dividing the drinkers into categories according to the number of drinks consumed per day [<1 alcoholic unit (A.U.); 1–2 alcoholic unit; >2 alcoholic unit], we could observe that Hcy was significantly related to the amount of drinks consumed [<1 A.U.: 10 (9.5–10.5); 1–2 A.U.: 11.4 (10.6–12.3); >2 A.U.: 11.7 (10.7–12.7) $\mu\text{mol/L}$; p for trend <0.05] whereas no relationship between vitamin B6 and alcohol was observed. Moreover, when analyses according to the drinking pattern were performed, we could demonstrate that the influence of alcohol on Hcy levels remained to be significant only among wine drinkers (p for trend <0.05) but not among beer drinkers ($p = 0.9$).

Conclusions: This study indicates that alcohol consumption determines a significant increase of Hcy levels, whereas no significant difference for lipoprotein(a) and B-group vitamins has been reported. The present findings seem to confirm previous findings of a positive significant relationship between wine, but not beer, consumption and Hcy plasma levels.

120 A NOVEL MUTATION IN THE LIPASE MATURATION FACTOR 1 (LMF-1) GENE RESPONSIBLE OF SEVERE HYPERTRIGLYCERIDEMIA

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Mutations in LPL, APOC2 or APOA-V genes are recognized causes of inherited forms of severe hypertriglyceridemia but most hypertriglyceridemic patients do not have mutations in any of these genes involved in the regulation of plasma TG levels. Recently several proteins have been shown to cooperate with LPL, either by favouring its maturation or by stabilizing it. An important task is to identify mutations in new candidate genes responsible for severe hypertriglyceridemia. Here we describe a novel mutation in the Lipase Maturation Factor 1 (LMF-1) gene leading to severe hypertriglyceridemia. The proband is a 41-years old Tunisian man who was referred to our attention because of severe hypertriglyceridemia first noted at the age of 32 in the occasion of a first episode of pancreatitis. Since then plasma TG levels have been between 7.86 and 22.4 mmol/L and he had been suffering from two more episodes of acute pancreatitis. After the last episode of pancreatitis he developed Diabetes Mellitus that has been controlled with insulin treatment. Mutations in the LPL, apoA5 and apo CII genes had been ruled out. The analysis of the LMF-1 gene shows the presence of a homozygous G to A substitution in the exon 9 (c.1391G>A), leading to a premature stop codon (W464X) responsible of a truncated LMF-1 protein. In conclusion, LMF1 should be considered an important candidate gene in those forms of severe hypertriglyceridemia that remains unexplained by mutations in the current set of candidate genes.

121 LP(a): A POSSIBLE LINK WITH MIGRAINE

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Background: Migraine, a common multifactorial neurovascular disorder, has been suggested to be an independent risk factor for stroke and data from literature evidenced that elevated lipoprotein(a) [Lp(a)] concentrations represent a risk factor for stroke. Aim of our study was to evaluate the role of Lp(a) in affecting migraine, so possibly contributing to identify a biological marker of predisposition to the disease.

Materials and Methods: Lp(a) levels have been detected in 138 migraine patients (110 females and 28 males), among whom 90 with aura, and 120 healthy subjects (87 females and 25 males), comparable for age and gender. Plasma levels of Lp(a) have been determined by an ELISA method.

Results: Median value of Lp(a) was 104 (1–2110) mg/L in migraine patients and 103 (9–695) mg/L in the control group ($p = 0.8$). A significant difference among tertiles of Lp(a) concentrations between patients and controls was found ($p = 0.04$). In particular, a significant difference in the high tertile of Lp(a) between patients and controls was observed ($p = 0.001$). Moreover, abnormal Lp(a) levels, defined as >300 mg/L, have been observed to influence significantly the predisposition to migraine [OR 3.4, 95%CI 1.57–7.55, $p = 0.002$], after adjustment for age, gender and traditional risk factors. No difference in Lp(a) concentrations was observed between patients with aura and without aura, and no relationship was found between abnormal Lp(a) concentrations and headache intensity.

Conclusions: The present study evidences a role for Lp(a) in affecting the risk of migraine, so providing information on a novel possible mechanism involved in the predisposition to the disease.

122 RELATIONSHIP OF SERUM GAMMA-GLUTAMYLTRANSFERASE WITH ATHEROGENIC DYSLIPIDEMIA AND GLYCEMIC CONTROL IN TYPE 2 DIABETES

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Background and Aims: Recently, it has been reported a strong interaction between serum gamma-glutamyltransferase (GGT) activity levels and obesity on the future risk of type 2 diabetes. Given the potential clinical importance of an interaction between obesity and serum GGT levels in predicting type 2 diabetes, we examined possible interactions between serum GGT levels and obesity and their effects on the prevalence rates of poor glycemic control and other common comorbidities of type 2 diabetes.

Methods and Outcome measures: We assessed whether the associations of body mass index (BMI) with hypertension (i.e., $>140/90$ mmHg or treatment), atherogenic dyslipidemia (triglycerides >1.7 mmol/L and/or HDL-cholesterol <1.04 mmol/L or treatment), hypercholesterolemia (LDL cholesterol >4.13 mmol/L or treatment), poor glycemic control (HbA1c $>6.5\%$) and hyperuricemia (>0.416 mmol/L in men and >0.386 in women or treatment) differed according to serum GGT levels in an outpatient cohort of 3,633 type 2 diabetic adults.

Results: Even though the associations of BMI with different outcome measures were significant, the associations varied remarkably by quartiles of GGT levels. As GGT levels increased, the association of BMI with atherogenic dyslipidemia and glycemic control strengthened ($p = 0.01$ and 0.004 for interactions, respectively); in contrast, the association of BMI with hypertension, hypercholesterolemia and hyperuricemia did not change across GGT quartiles. For example, within the lowest GGT quartile, BMI was not associated with atherogenic dyslipidemia or worse glycemic control, in contrast to the highest GGT quartile, wherein the prevalence rates ranged from 62.3% to 74.7% for dyslipidemia, and from 75.3% to 83% for glycemic control, respectively. Notably, the results remained unchanged after adjustment for gender, age, alcohol consumption, diabetes duration and treatment. Almost identical results were found when participants, who were light to moderate drinkers, were excluded from analysis.

Conclusions: Our findings indicate that BMI is associated with worse glycemic control and atherogenic dyslipidemia only among those with high-normal serum GGT activity, but not in those with low-normal serum GGT activity levels. These findings suggest that obesity itself may not be a sufficient risk factor for atherogenic dyslipidemia or worse glycemic control in people with type 2 diabetes. Future prospective cohort studies are needed to confirm if the interaction between BMI and serum GGT may be useful for identifying a high-risk subpopulation of type 2 diabetic patients.

123 THE NEGATIVE CORRELATION BETWEEN FLOW-MEDIATED DILATION (FMD) AND ARTERIAL SIZE MAY BE ASCRIBED TO A MATHEMATICAL ARTEFACT

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The use of variables computed as a ratio of two measures, especially in correlation/regression analysis, has been repeatedly criticized by statisticians. The brachial artery Flow-Mediated Dilation (FMD%), a non invasive marker of endothelial function widely applied in clinical studies, is a typical ratio variable, being calculated as: (absolute diameter change after stimulus)/(resting diameter) $\times 100$. Unsurprisingly, significant correlations between FMD% and resting diameter have been repeatedly reported, with coefficients ranging from -0.2 to -0.8 . These correlations have been tentatively explained by a variety of biological reasons, but instead they may be largely accounted by a mathematical artefact called mathematical coupling.

To test this hypothesis we used a Monte-Carlo approach by computing a simulated FMD% in which the numerator and the denominator were lacking of any real biological or physical relation. We started from real measurements of resting diameters and of diameter changes obtained from 189 patients with cardiovascular risk factors attending the Monzino Cardiologic Centre in Milan. To disrupt the biological link between the two variables, we created a dataset of virtual patients by randomly coupling the resting diameter with the diameter change belonging to different subjects. FMD% was then computed from the two unrelated measures according to the above formula. The random coupling was reiterated 1000 times. The overall mean correlation coefficient between simulated FMD% and resting diameter was -0.170 (95% confidence interval $-0.166, -0.174$), a value very close to that observed in the original data (-0.168), and in the same range of those reported in the literature. These results indicate that the correlation between FMD% and artery size at rest is likely due to mathematical coupling.