**Hypothesis:** Since the larger part of plasma C3 is derived from liver and the presence fatty liver is, by itself, related to CAD, we hypothesize that the relation between C3 and CAD may be related to presence of fatty liver.
**Materials**: The relation between C3, CAD and an indicator of fatty liver (plasma ALT concentration) was studied in the CODAM study (Cohort on Diabetes and Atherosclerosis Maastricht). This cohort consists of 301 normal glucose tolerant, 127 impaired glucose tolerant and 146 type 2 diabetes mellitus (T2DM) subjects, invited from a large population-based cohort on basis of an elevated risk for T2DM. The relation between C3 and a self-reported history of CAD (defined as myocardial infarction, bypass surgery of the coronary arteries, balloon dilatation and / or stent placement) was evaluated by logistic regression. The relation between plasma C3 and fatty liver was evaluated in linear regression analysis.
**Results**: Plasma C3 levels were significantly associated with increased CAD prevalence, also after adjusting for age, gender, smoking and glucose tolerance status (model 1, OR per unit C3 is 3.2 [95% CI: 1.6–6.5], p<0.001). Additional adjustment for known CAD risk factors showed that this relation was independent of: the metabolic syndrome, markers of inflammation (CRP, VCAM, ICAM, IL-6), markers of lipid metabolism (total and HDL-cholesterol and triglycerides), and markers of an acute phase / complement response (C4, ceruloplasmin, haptoglobin, transferrin, serum amyloid A). It was, however, affected by fasting insulin level (OR C3 is 2.1 ([CI 95% 1.0–4.6], p= 0.06), with a significant contribution of insulin in this model (p=0.011). The partial correlation between C3 and ALT was 0.364 (p<0.001; adjusted for age, gender, alcohol intake and glucose tolerance status). This association was affected by adjustment for fasting insulin but not, or considerably less, by adjustment for markers of inflammation, lipid metabolism, acute phase response / complement or kidney function. These data imply that the relation between insulin and C3 is affected by the presence of fatty liver, or vice versa. However, when the association between C3 and CAD (as shown in model 1) was additionally adjusted for ALT, the association between C3 and CAD was not substantially affected (OR is 3.2 [95% CI: 1.5–6.8], p<0.002).
**Conclusion**: Both the association between plasma C3 levels and CAD, and the relation between plasma C3 levels and fatty liver (as represented by plasma ALT) were, at least partly, explained by insulin and/or insulin resistance, but adjustment for ALT did not affect the relation between C3 and CAD. The data suggest that hyperinsulinemia and/or insulin resistance, rather than fatty liver by itself, explain part of the CAD risk associated with high levels of plasma C3.
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## 1217

**Low-grade inflammation and cardiovascular risk in the metabolic syndrome: the CODAM study**
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**Background:** The Metabolic Syndrome (MetS) is associated with an increased risk for cardiovascular disease and type 2 diabetes (T2DM). Abdominal obesity, dyslipidemia, hypertension and insulin resistance are the main determinants that define the MetS, but low-grade inflammation is also increasingly recognized as an underlying trait in the cardiovascular risk associated with the MetS.
**Aim**: To identify inflammation markers that are determinants of coronary heart disease (CHD) and to establish their association with the individual criteria of the metabolic syndrome.
**Methods**: The CODAM (Cohort study Diabetes and Atherosclerosis Maastricht) cohort was used. The cohort includes 574 subjects who were invited from a large population based cohort on basis of an elevated risk for T2DM. As determined by oral glucose tolerance test, 301 subjects were normal glucose tolerant, 127 were impaired glucose tolerant or had impaired fasting glucose levels and 146 had T2DM. Relevant anthropometric and blood parameters were determined. First, inflammation markers were identified that were elevated in subjects with a self-reported history of CHD. Subsequently, logistic regression analyses was used to determine if the relation between the inflammation markers and CHD was independent of the MetS. Finally, the relations between the inflammation makers and the individual determinants of the MetS were determined in linear regression analyses.
**Results**: C-reactive protein (CRP), interleukin 6 (IL6) and soluble vascular cell adhesion molecule (VCAM) were elevated in CHD. Logistic regression showed that the MetS was a significant determinant of CHD (odds ratio [$OR_{MetS}$] is 1.82, $P_{MetS}$: 0.019 adjusted for age, gender and glucose tolerance status). Addition of IL6 to the above described logistic regression model, reduced the association of MetS with CHD ($OR_{MetS}$: 1.62, $P_{MetS}$: 0.064; $OR_{IL6}$: 3.05, $P_{IL6}$: 0.005). Analysis with CRP resulted in similar results ($OR_{MetS}$: 1.64, $P_{MetS}$: 0.056; $OR_{CRP}$: 1.78, $P_{CRP}$: 0.061). On the other hand, addition of VCAM to the model did not affect the association of MetS and CHD ($OR_{MetS}$: 1.78, $P_{MetS}$: 0.026; $OR_{VCAM}$: 43.8, $P_{VCAM}$: 0.001). Multiple linear regression adjusted for age, gender and glucose tolerance status showed that CRP, IL6 and VCAM were all independently associated with lipids and HOMA-IR ($P_{CRP}$: 0.039, $P_{IL6}$: 0.035, $P_{VCAM}$ <0.001). CRP (P<0.001) and IL6 (P<0.001) were also associated with waist circumference. Only CRP was related to blood pressure.
**Conclusion**: MetS was a significant determinant of CHD. This relation was reduced if CRP or IL6 were included in the model, and remained unaltered if VCAM was added. CRP and IL6 were mainly associated with waist and lipids, whereas VCAM was associated with insulin resistance and lipids. Our data suggest that low-grade inflammation may be an important pathway linking the MetS to CHD. Furthermore it suggests that the association of CRP and IL6 with CHD may occur via a different mechanism than between VCAM and CHD.
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## 1218

**Metabolic syndrome and goals of therapy for cardiovascular disease (CVD) risk**
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**Background and Aims**: Metabolic Syndrome (MS) is a cluster of risk factors for CVD. Recently, goals of therapy of blood pressure, glucose, and lipids were defined, categorizing patients with MS in 3 classes of Framingham-based estimates of 10 yr-CVD risk: low-to-moderate risk (<10%), moderately high risk (10–20%), and high CVD risk (>20%). Aim of this study is to verify the achievement of treatment goals in patients with MS.
**Materials and Methods**: A cohort of 2945 individuals, with no history of diabetes, living in Florence and in the nearby Bagno a Ripoli municipality, enrolled in a screening program for diabetes, were studied. Of these, 672 (aged 60.5±9.7 yrs, BMI 29.5±4.0 kg/$m^2$) were affected by MS according to the revised (2004) National Cholesterol Education Program (NCEP) criteria. Anthropometric measures, smoking habits, glucose tolerance (120 minutes after a 75 g oral glucose load), lipid profile, and blood pressure were assessed. 10 yrs CVD risk was computed by Framingham score model based on sex, age, smoking, systolic and diastolic blood pressure, total HDL cholesterol, and diabetes.
**Results**: 281 (41.8%) subjects had a low to moderate CVD risk, 187 (27.8%) a moderately high risk, and 204 (30.3%) a high CVD risk; normal weight was observed in 9.4% of subjects of the first class, 11.2% in the second class, and only 7.3% in the high risk class. Coronary heart disease (CHD) at enrolment was observed in 5.6% subjects. Considering LDL cholesterol, levels<130 mg/dl were found in 47.0% and 44.9% subjects with low to moderate and moderately high risk, respectively, while LDL levels<100 mg/dl were found in only 13.7% of high risk patients. CHD patients with LDL<70 mg/dl were 5.4%, and those with non-HDL cholesterol<100 mg/dl were 2.6%. The prevalence of non-HDL cholesterol<160 mg/dl was 46.3% in low risk individuals and 40.6% in subjects with moderately high risk class. Few patients were treated with lipid drugs as statins, fibrates or fish oil: 3.5% in the low risk, 4.3% in the medium risk class, and only 6.4% in the high risk class. Patients with blood pressure<130/80 mm Hg were 44.8% and 24.0% in low and moderately high risk, respectively, while high risk subjects with optimal blood pressure control were 14.7% only. 423 (62.9%) subjects had normal glucose tolerance, 119 (17.7%) impaired glucose tolerance, and 140 (20.8%) type 2 diabetes; fasting plasma glucose>100 mg/dl was found in 24.9% of low risk subjects, 18.2%