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<table>
<thead>
<tr>
<th>Name</th>
<th>Seite</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beer S</td>
<td>3</td>
</tr>
<tr>
<td>Berthoud M</td>
<td>3</td>
</tr>
<tr>
<td>Brun N</td>
<td>3</td>
</tr>
<tr>
<td>Darioli R</td>
<td>3</td>
</tr>
<tr>
<td>Depairon M</td>
<td>3</td>
</tr>
<tr>
<td>Drexel H</td>
<td>4</td>
</tr>
<tr>
<td>Gruber M</td>
<td>4</td>
</tr>
<tr>
<td>Mazzolai L</td>
<td>4</td>
</tr>
<tr>
<td>Meier N</td>
<td>4</td>
</tr>
<tr>
<td>Mono M.-L.</td>
<td>5</td>
</tr>
<tr>
<td>Moser A</td>
<td>5</td>
</tr>
<tr>
<td>Nanchen D</td>
<td>5</td>
</tr>
<tr>
<td>Ochs N</td>
<td>5</td>
</tr>
<tr>
<td>Prior J.O.</td>
<td>8</td>
</tr>
<tr>
<td>Saely C.H.</td>
<td>9, 10</td>
</tr>
<tr>
<td>Vonbank A</td>
<td>10</td>
</tr>
<tr>
<td>Wittwer J</td>
<td>10</td>
</tr>
<tr>
<td>Romanens M</td>
<td>9</td>
</tr>
<tr>
<td>Rodondi N</td>
<td>9</td>
</tr>
</tbody>
</table>
The metabolic syndrome, angiographically determined stable coronary artery disease, and subclinical inflammation

Beer S., Rein P., Saely C.H., Vorbank A., Woess M., Boehnel C., Jankovic V., Dravet H. (Feldkirch)

Background: The metabolic syndrome (MetS) and stable coronary artery disease (CAD) frequently co-occur; the individual contributions of these entities to subclinical atherosclerosis have not been investigated yet.

Objective: We therefore aimed at investigating markers of inflammation in patients with the MetS, in patients with CAD, and in patients who had both, the MetS and CAD.

Methods: We enrolled 935 consecutive patients undergoing coronary angiography for the evaluation of suspected or established stable CAD. The MetS was defined according to National Cholesterol Education Programme Adult Treatment Panel III criteria; coronary stenoses with lumen narrowing ≥50% were considered significant.

Results: From our patients 520 (55.6%) had significant coronary stenoses; the prevalence of the MetS was higher in our patients with significant stenoses than in those without such lesions (0.44 ± 0.51 vs. 0.37 ± 0.54 mg/dl; p = 0.004 and 7.1 ± 1.8 vs. 6.4 ± 1.8 mg/dl; p = 0.001, respectively). In contrast, these inflammatory markers were not significantly elevated in patients with significant stenoses among subjects with the MetS (p = 0.776 and p = 0.713, respectively) nor among those who did not have the MetS (p = 0.882 and p = 0.119, respectively). Similar results were obtained with the International Diabetes Federation definition of the MetS.

Conclusions: We conclude that subclinical inflammation is strongly and significantly associated with the MetS but not with angiographically determined stable CAD.

Are the guidelines appropriate for the global cardiovascular risk assessment among adult women in Switzerland?

Berthoud M., Stauffer I., Depairon M., Darioli R. (Lausanne)

The primary prevention of cardiovascular diseases (CVD) is based on the individual risk assessment by using Framingham and similar algorithms derived mainly from US or European male populations. The purpose of this prospective study was to compare the appropriateness of three different common guidelines for cardiovascular risk stratification when using subclinical-atherosclerosis as a surrogate of CV risk. The study population included 560 women (W), aged from 20 to 65 years, non diabetic and without established CVD, who were consecutively referred to our Lipid Clinic for therapeutic advices. CV-risk factors were systematically screened for each subject, including medical history, physical examination and clinical chemistry. Their estimated 10-year CV-risk assessment was performed using the guidelines of Swiss AGLA (AGLA), NCEP-ATP-3 (ATP-3) and 3th JES-ESC (ESC) guidelines (GL). B-mode ultrasound on carotid and femoral arteries was performed to detect carotids plaques (focal thickening of intima-media ≥1.2 mm). W with plaques on ≥2 carotid and/or femoral sites were considered as high CV risk (HR). The proportions of W stratified as high 10-year CV-risk by the GL were the following: 5% (AGLA), 2% (ESC) and 24% (ESC). The comparative values (area under the ROC-curve) of GL to detect the 160 HR-W with subclinical-atherosclerosis were: GAGA >0.78, GES > 0.68, GES > 0.77. In conclusion, the results suggest that current AGLA-GL recommended by the Swiss Society of Cardiology are the most appropriate to identify HR-W requiring more intensive therapy for the primary prevention of CVD.

Report of 5-year experience of dyslipidemia management in children

Brun N., Alloguy Y., Girardin E. (Genève)

There is convincing evidence that atherosclerotic process begins in childhood and is enhanced in case of associated lipid abnormalities. With the epidemic of obesity in children, prevalence of lipid abnormalities is increasing, leading to accelerated atherosclerotic process in adulthood. Primary prevention of cardiovascular disease by lifestyle modifications and statin therapy in high-risk children is widely recommended. We retrospectively studied children referred to the Lipid Clinic in the Children Hospital of Geneva from 2002 to 2007. Age at referral, aetiology, co-existence of additional cardiovascular risk factors, work-up and management were studied. Of the 73 children collected, 44% have a monogenic hypercholesterolemia, 30% a polygenic hypercholesterolemia, 12% a secondary hypercholesterolemia and 14% other dyslipidemia. High-risk group was defined as LDL-C levels >4.9 mmol/l or HDLC levels >1.2 mmol/l associated with severe familial history of atherosclerosis. In the high-risk group, vascular exploration (measurement of intima-media-thickness and research of endothelial dysfunction) was performed in the children older than 6-year-old. Anomalies in intima-media-thickness were found in 13 of the 18 children examined, with evidence of endothelial dysfunction in eight of them. The metabolic syndrome (MetS) was introduced in 19/37 children in the high-risk group, in accordance with the new recommendations from the American Heart Association. No secondary effects, except slight elevations of plasmatic creatine kinase level, were observed. Stabilisation or even regression of irregularities of the carotid wall were documented during the cardiac follow-up. These data showed that targeted tracking is mandatory already in childhood. More awareness of paediatric predictors of atherosclerosis is needed among physicians, in order to moderate the burden of cardiovascular disease in the next generation. Criteria for risk stratification upon lipid levels are still lacking in children and statins are to be reserved only to high risk group with careful follow-up.

Trends in disability related to cardiovascular diseases in Switzerland between 1987 and 2006

Darioli R., Prior J., Perdrix J. (Lausanne)

Cardiovascular diseases (CVD) sustain a major cause of morbidity and mortality in industrialized countries. However, little attention is done on disability associated with CVD.

Objectives: The objective of this study was to evaluate the trends of disability linked to CVD during these last 20 years in Switzerland. Based on medical publications and official Swiss statistics, CVD accounted for only 2.3% among all medical causes of sickness certification for ≥6 days established by primary care physicians in patients aged 15 to 64 years. Furthermore in 2006, CVD were involved only in 1.5% of women and 5.5% of men receiving a pension of Swiss disability insurance. Between 1987 and 2006, the proportion of diagnosis of CVD at medical office decreased from 14.6 to 12.4% (~15%), while during the same period, the reduction of the proportion of disability pension was more pronounced, from 9.6 to 4.1% (~57%).

Conclusion: These results demonstrate that, despite the large number of CVD in Swiss population and the progressive increase of disability pensions for all causes during the last 20 years, a significant reduction of disability pensions due to CVD, and consequently result in large decrease of health costs among active population.

Prevalence of sub-clinical atherosclerosis across age and gender in West of Switzerland

Depairon M., Stauffer I., Berthoud M., Darioli R. (Lausanne)

Atherosclerosis (ATs) is a focal and disseminated disease of arterial wall with asymptomatic progression for many years until its first clinical manifestation occurs, such as an acute coronary syndrome or a stroke. Since more than 50% of victims of a first cardiovascular event (CVE) were stratified with a coronary risk of less than 20%, clinicians should consider other tests to identify high risk patients. Among them, B-mode carotid ultrasound was developed to predict the risk of CVE beyond the traditional RF assessment alone. However, epidemiological data on subclinical atherosclerosis are lacking. The purpose of this prospective study was to evaluate the prevalence of subclinical atherosclerosis on femoral and carotid atherosclerosis across age and gender among adults. The study population included 1620 asymptomatic patients aged from 20–70 y (mean ± SD = 48 ± 12 y), without established CVD, who were consecutively referred from Western Switzerland for therapeutic advice. Cardiovascular risk factors (CV-RF) were systematically screened for each subject, including medical history, physical examination and clinical chemistry. B-mode ultrasound was performed on carotid and femoral arteries by two investigators to detect atherosclerotic plaques (defined as focal thickening of intima-media ≥1.2 mm). The prevalence of ATs increased with age from 6 to 78% (mean = 61%) in men and from 6% to 89% (mean = 48%) in women, respectively (p <0.001). Furthermore, there was a significant correlation with the number of the traditional CV-RF (r = 0.31, p <0.001). However, no ATs was detected in 30% of patients with ≥3 CV-RF. As illustrated in the table 1, there was an increased prevalence of ATs across age in both genders (p <0.001). However, in contrary to general belief, not all persons aged ≥50 y had ATs. In conclusion, the results indicate that beyond the epidemiology of the traditional CV-RF, more research should be performed on subclinical ATs in order to improve the primary prevention of CVD.
Lipid predictors of cardiovascular events in statin-treated coronary patients with type 2 diabetes

Drexel H., Aczel S., Marte T., Vonbank A., Saely C.H. (Feldkirch)

Background: Vascular risk in diabetic patients remains high despite statin treatment.

Objective: We aimed at identifying which lipid parameters drive vascular risk in this important patient population despite statin treatment.

Methods: We recorded vascular events over 5.6 years in 491 consecutive statin-treated patients with angiographically proven stable CAD, covering 2750 patient-years.

Results: From our patients 116 (23.6%) had type 2 diabetes (T2DM). In the total cohort, low HDL cholesterol (standardized adjusted hazard ratio (HR) 0.73 [0.60–0.89]; p = 0.001), low apolipoprotein A1 (HR 0.77 [0.65–0.92]; p = 0.003) a small LDL particle diameter (0.76 [0.64–0.91]; p = 0.002), and high triglycerides (1.20 [1.05–1.38]; p = 0.007) significantly predicted vascular events, but not total cholesterol (p = 0.995), LDL cholesterol (p = 0.961), or apolipoprotein B (p = 0.877). Patients with T2DM were at a significantly higher vascular risk than non-diabetic subjects (38.6% vs. 24.1%; p < 0.001). Importantly, like in the total population, low HDL cholesterol (HR = 0.58 [0.41–0.82]; p = 0.002), low apolipoprotein A1 (HR = 0.70 [0.51–0.95]; p = 0.022), a small LDL particle diameter (0.67 [0.50–0.91]; p = 0.013), and high triglycerides (1.30 [1.11–1.53]; p = 0.001) drove vascular risk in our statin treated coronary patients with T2DM, whereas total cholesterol (p = 0.822), LDL cholesterol (p = 0.233), and apolipoprotein B (p = 0.366) did not.

Conclusions: The pattern of low HDL cholesterol, low apolipoprotein A1, small LDL particles, and high triglycerides is the main lipid risk factor in statin treated coronary patients with T2DM.

Diagnostic and prognostic impact of plasma lipids in patients with lower respiratory tract infection – an observational study

Gruber M., Christ-Crain M., Keller U., Mueller B., Schmutz P. (Basel)

Background: Changes in plasma lipids and particularly a decrease in HDL cholesterol levels are associated with adverse clinical outcomes in critically ill and septic patients. The prognostic or diagnostic utility of plasma lipids in patients with less severe systemic infections is unknown.

Materials and methods: We pooled data from patients with lower respiratory tract infections (LRTI) enrolled in four randomized trials. We studied the time course of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and triglycerides (TG) and compared it with other markers of inflammation, diagnosis and medical outcomes.

Results: Of the 572 included patients, 372 had community-acquired pneumonia (CAP), 200 other lower respiratory tract infections (LRTI) including bronchitis and 100 other lower respiratory tract infection – an observational study.

Coronary patients with type 2 diabetes

Mazzolai L., Aubert J-F., Bouzourene K., Pelliegini M., Hayoz D., Nussberger J. (Lausanne, Lausanne and Fribourg)

Hypertension is associated with increased risk of cardiovascular diseases. Antihypertensive treatment, particularly blockade of the renin-angiotensin system (RAS), contributes to prevent atherosclerosis-mediated cardiovascular events. Direct comparison of different antihypertensive treatments on atherosclerosis characteristics was sparse. ApoE-/- mice with vulnerable (2K1C renovascular hypertension model) or stable (1K1C renovascular hypertension model) atherosclerotic plaques were used. Mice were treated with either: aliskiren (renin inhibitor), irbesartan (angiotensin-receptor blocker), atenolol (beta-blocker) or amlodipine (calcium-channel blocker). Atherosclerosis characteristics were assessed. Hemodynamic and hormonal parameters measured. Aliskiren and irbesartan significantly prevented atherosclerosis progression in 2K1C mice. Indeed, compared to untreated animals plaques showed: thinner fibrous cap and macrophage content [p < 0.05], smaller lipid core [p < 0.05], decreased media degeneration, layering and macrophage content [p < 0.05] and increased smooth muscle cell (SMC) content [p < 0.05]. Interestingly, Aliskiren significantly increased SMC compared to irbesartan. Despite similar blood pressure lowering, only partial plaque stabilization was attained by atenolol and amlodipine. Amlodipine increased plaque SMC content [p < 0.05] while atenolol decreased plaque inflammation [p < 0.05]. This divergent effect was also observed in 1K1C mice. Specific RAS blockade prevents atherosclerosis progression. First evidence is provided that direct renin inhibition mediates athero-protective plaque stabilization. In contrast, beta-blocker and calcium-channel blocker treatment only partially stabilize plaques differentially influencing atherogenesis. Angiotensin II decisively mediates plaque vulnerability.

Prior statin use, intracranial hemorrhage and outcome after intra-arterial thrombolysis for acute ischemic stroke

Meier N., Nedelj C., Fitev K., Cikovic I., Dugas J., Feldkirch O., Remonda L., Schroth G., Mattle H.P., Arnold M. (Bern)

Background: There is only limited data on whether prior statin use and/or cholesterol levels are associated with intracranial hemorrhage (ICH) and outcome after intra-arterial thrombolysis (IAT).
Purpose: To evaluate the association of statin pre-treatment and cholesterol levels with the overall frequency of ICH, the frequency of symptomatic ICH, and clinical outcome at 3 months.

Methods: We analyzed 311 consecutive patients (mean age 63 years, 43% women) who received IAT.

Results: Statin pre-treatment was present in 18%. Patients on statins were older (67 vs. 62 years, p = 0.015) and suffered more often from hypertension (83% vs. 57%, p < 0.001), coronary artery disease (80% vs. 37%, p = 0.001), and previous transient ischemic attacks (26% vs. 9%, p < 0.001). The overall frequency of ICH was 20.6% and of symptomatic ICH 4.8%. The incidence of any ICH (34.5% vs. 17.6%, p = 0.005) and symptomatic ICH (10.9% vs. 3.5%, p = 0.02) was higher among patients receiving statins before IAT. Plasma cholesterol levels were not associated with ICH. After multivariate analysis, prior statin use, but not cholesterol levels on admission, is not associated with clinical outcome at 3 months.

Conclusion: Prior statin use, but not cholesterol levels on admission, is associated with the overall frequency of ICH and with symptomatic ICH after IAT without impact on clinical outcome.

Carotid arteriosclerotic plaque morphology may predict the intracerebral ischemic lesion load: a 3 Tesla MRI study


Background and purpose: Carotid atherosclerosis is a major cause of stroke. Traditionally, the degree of stenosis has been used to assess the risk of thromboembolism originating from an atherosclerotic plaque. Recent data suggest that the total volume and the histological composition of the plaque might also be related to plaque vulnerability. We set out to determine the association between plaque morphology features and the cerebral ischemic lesion load in the territory of the corresponding carotid artery.

Patients and methods: Ten patients (8 men and 2 women, mean age 67 y) underwent a high-field (3 Tesla) MRI of the carotid bifurcation and the brain. A pre-specified protocol including T1-, T2-, and intermediate-weighted fast spin echo sequences and FLAIR sequences was used. The following morphology features were correlated with the number of ischemic lesions in the territory of the corresponding carotid artery as seen on the FLAIR images of the brain: intraplaque hemorrhage, thin or disrupted fibrous cap, large lipid core.

Results: Four patients had a stenosis of the right internal carotid artery (ICA), five patients a stenosis of the left ICA, and one patient had a non-stenotic atherosclerotic plaque of both carotid arteries. There were 4 severe (high grade), 1 moderate and 4 lower grade stenoses. The carotid stenosis was symptomatic in 3 patients and asymptomatic in the remaining 7 patients. Four of the 7 patients with asymptomatic stenoses had silent ischemic lesions on brain MRI. There was a weak correlation between the presence of a large lipid core and the ischemic lesion load in the corresponding brain territory (r = 0.266). Neither the degree of stenosis, nor the presence of thin/disrupted fibrous cap or intraplaque hemorrhage were correlated to the intracerebral ischemic lesion load.

Conclusion: These preliminary results, although very preliminary, suggest that the presence of a large lipid core may help to identify vulnerable atherosclerotic plaques.

The role of caveolae and clathrin in apoA-I/HDL transport through endothelial cells

Moser A., Zemp M., Fuchs S., Caverlier C., Rohrer L., von Eckardstein A. (Zürich)

Plasma levels of high density lipoproteins (HDL) and its main apolipoprotein A-I (apoA-I) are inversely correlated with the risk of atherosclerotic cardiovascular disease. However, it is unclear how apoA-I and HDL are transported across the endothelium from the lumen into the vascular wall. Clathrin- and caveolae-mediated endocytosis are the predominant endocytic pathways. Clathrin has been shown to be involved in the uptake of LDL. Caveolae are highly abundant in endothelial cells.

Purpose: The aim is to determine the role of caveolin-1 and clathrin in transporting apoA-I and HDL through endothelial cells.

Methods: Endothelial cells expressing caveolin-1 specific small-hairpin RNA (shRNA) or endothelial cells transfected with clathrin specific small-interference RNA (siRNA) are analyzed by real-time PCR and Western Blot. Their transport capacity is tested by incubation with radiolabeled apoA-I and HDL.

Results: Silencing significantly down-regulated the mRNA and protein expression of caveolin-1 and clathrin. Furthermore, we found that cell association of apoA-I is reduced after silencing of caveolin-1 but not of clathrin. The binding, internalisation and transport capacities will be further evaluated.

Eligibility for statin therapy in primary prevention: discrepancies using different guidelines in a population-based study in Switzerland


Introduction: Recommendations for statin use for primary prevention of coronary heart disease (CHD) are based on estimation of the 10-year CHD risk. We compared the 10-year CHD risk assessments and eligibility percentages for statin therapy using three scoring algorithms currently used in Switzerland.

Methods: We studied 5683 women and men, aged 35–75, without overt cardiovascular disease (CVD), in a population-based study in Lausanne, Switzerland. We compared the 10-year CHD risk using three scoring schemes, i.e., the Framingham risk score (FRS) from the U.S. National Cholesterol Education Program’s Adult Treatment Panel III (ATP III), the PROCAM scoring scheme from the International Atherosclerosis Society (IAS), and the European risk SCORE for low-risk countries, without and with extrapolation to 60 years as recommended by the European Society of Cardiology guidelines (ESC). With FRS and PROCAM, high-risk was defined as a 10-year risk of fatal or non-fatal CHD>20% and a 10-year risk of fatal CVD> 5% with SCORE. We compared the proportions of high-risk participants and eligibility for statin use according to these three schemes. For each guideline, we estimated the impact of increased statin use from current partial compliance to full compliance on potential CHD deaths averted over 10 years, using a success proportion of 27% for statins.

Results: Participants classified at high-risk (both genders) were 5.8% according to FRS and 3.0% to the PROCAM, whereas the European risk SCORE classified 12.5% at high-risk (15.4% with extrapolation to 60 years). For the primary prevention of CHD, 18.5% of participants were eligible for statin therapy using ATP III, 16.6% using IAS, and 10.3% using ESC (13.0% with extrapolation) because ESC guidelines recommend statin therapy only in high-risk subjects. In comparison with IAS, agreement to identify eligible adults for statins was good with ATP III, but moderate with ESC (Figure). Using a population perspective, a full compliance with ATP III guidelines would reduce up to 17.9% of the 24’310 CHD deaths expected over 10 years in Switzerland, 17.3% with IAS and 10.8% with ESC (11.5% with extrapolation).

Conclusion: Full compliance with guidelines for statin therapy would result in substantial health benefits, but proportions of high-risk participants and eligible adults for statin use varied substantially depending on the scoring systems and corresponding guidelines used for estimating CHD risk in Switzerland.

Subclinical thyroid dysfunction is associated with the risk of coronary heart disease and mortality

Ochs N., Auer R., Bauer D.C., Nanchen D., Cornuz J., Gusseklo J., Rodondi N. (Lausanne, San Francisco, Leiden)

Background: Data on the association between subclinical thyroid dysfunction and CHD and mortality are conflicting.

Purpose: To summarize prospective evidence about the relationship between subclinical thyroid dysfunction and CHD and mortality.


Data synthesis: 12 prospective studies met eligibility criteria, 10 were population-based. Among the population-based studies with 14449 participants, 10 examined subclinical hyperthyroidism (2134 CHD events and 2822 deaths), and 5 studies examined subclinical hyperthyroidism (1392 CHD events)
Abb. 1
Forest Plots for Subclinical Hypothyroidism.
Abb. 2
Forest Plots for Subclinical Hyperthyroidism.
Objective: To investigate the association of the MetS with inflammation in this clinically important patient population. Methods: We enrolled 759 consecutive patients with angiographically proven stable CAD. Results: In univariate analyses, hsCRP was higher in patients with the MetS (ATP-III definition; n = 281) than in those who did not have the MetS (0.48 ± 0.86 vs. 0.41 ± 0.78 mg/dl; p < 0.001), and also was higher in patients who fulfilled the large waist (0.48 ± 0.57 vs. 0.39 ± 0.56 mg/dl; p < 0.001) and the low LDL (0.71 ± 1.16 vs. 0.37 ± 0.59 mg/dl; p < 0.001) criteria than in those who did not. Importantly however, after adjustment for age, gender, smoking and LDL cholesterol by means of analysis of covariance only the low HDL cholesterol criterion (F = 21.98; p < 0.001) remained significantly associated with hsCRP. The significant and independent association of low HDL with hsCRP was confirmed after additional adjustment for all other MetS traits (F = 23.59; p < 0.001).

Conclusions: We conclude that among patients with angiographically proven stable CAD, low HDL cholesterol drives the association between the MetS and subclinical inflammation. This observation is well in line with the paramount role of low HDL cholesterol as a marker of cardiovascular risk in this important patient population.

Key role of low HDL cholesterol for the association of the metabolic syndrome with inflammation in coronary patients


Background: The association of the metabolic syndrome (MetS) and of the individual MetS stigmata with inflammation in patients with established coronary artery disease (CAD) has not been investigated yet.

Objective: To investigate the association of the MetS with inflammation in this clinically important patient population.

Methods: We enrolled 759 consecutive patients with angiographically proven stable CAD. Results: In univariate analyses, hsCRP was higher in patients with the MetS (ATP-III definition; n = 281) than in those who did not have the MetS (0.48 ± 0.86 vs. 0.41 ± 0.78 mg/dl; p < 0.001), and also was higher in patients who fulfilled the large waist (0.48 ± 0.57 vs. 0.39 ± 0.56 mg/dl; p < 0.001) and the low LDL (0.71 ± 1.16 vs. 0.37 ± 0.59 mg/dl; p < 0.001) criteria than in those who did not. Importantly however, after adjustment for age, gender, smoking and LDL cholesterol by means of analysis of covariance only the low HDL cholesterol criterion (F = 21.98; p < 0.001) remained significantly associated with hsCRP. The significant and independent association of low HDL with hsCRP was confirmed after additional adjustment for all other MetS traits (F = 23.59; p < 0.001).

Conclusions: We conclude that among patients with angiographically proven stable CAD, low HDL cholesterol drives the association between the MetS and subclinical inflammation. This observation is well in line with the paramount role of low HDL cholesterol as a marker of cardiovascular risk in this important patient population.

Plaques in the common carotid artery are independent predictors of angiographically determined coronary atherosclerosis

Rein P., Kathrein T., Beer S., Vonbank A., Saely C.H., Drexel H. (Feldkirch)

Background: Atherosclerosis is a systemic disease. However, the association between the presence of common carotid artery (CCA) plaques and the presence of coronary artery disease is unknown.

Objective: The aim of this study was to examine whether common carotid artery (CCA) plaques are associated with angiographically determined coronary atherosclerosis.

Results: In univariate analyses, hsCRP was higher in patients with the MetS (ATP-III definition; n = 281) than in those who did not have the MetS (0.48 ± 0.86 vs. 0.41 ± 0.78 mg/dl; p < 0.001), and also was higher in patients who fulfilled the large waist (0.48 ± 0.57 vs. 0.39 ± 0.56 mg/dl; p < 0.001) and the low LDL (0.71 ± 1.16 vs. 0.37 ± 0.59 mg/dl; p < 0.001) criteria than in those who did not. Importantly however, after adjustment for age, gender, smoking and LDL cholesterol by means of analysis of covariance only the low HDL cholesterol criterion (F = 21.98; p < 0.001) remained significantly associated with hsCRP. The significant and independent association of low HDL with hsCRP was confirmed after additional adjustment for all other MetS traits (F = 23.59; p < 0.001).

Conclusions: We conclude that among patients with angiographically proven stable CAD, low HDL cholesterol drives the association between the MetS and subclinical inflammation. This observation is well in line with the paramount role of low HDL cholesterol as a marker of cardiovascular risk in this important patient population.

Key role of low HDL cholesterol for the association of the metabolic syndrome with inflammation in coronary patients

Methods: A total of 194 patients undergoing coronary angiography for the evaluation of established or suspected stable coronary artery disease (CAD) were included. Each patient underwent carotid arterial ultrasound examination. The presence of focal plaques in the CCA was recorded. Coronary stenoses with luminal narrowing ≥50% were considered significant.

Results: From our patients, 55.7% had significant CAD, and plaques in the CCA were present in 34.5%. The prevalence of significant coronary stenoses was significantly higher in patients with plaques in the CCA than in patients who did not have such plagues (76.1% vs. 44.9%; p <0.001). In logistic regression analysis adjusting for age, gender, body mass index, blood pressure, diabetes, smoking, LDL cholesterol, HDL cholesterol, plaques of the CCA proved significantly and independently predictive of significant stenoses at angiography, with an odds ratio of 3.50 (95% CI 1.62–7.54); p = 0.001.

Conclusion: Common carotid artery plaques are independently predictive for the presence of angiographically determined CAD.

Prediction of coronary heart disease with markers of atherosclerosis and of inflammation


Background: Several markers of atherosclerosis and of inflammation have been shown to predict coronary heart disease (CHD) individually. However, the utility of markers of inflammation and of inflammation on prediction of CHD over traditional risk factors has not been well established, especially in the elderly.

Methods: We studied 2202 men and women, aged 70–79, without baseline cardiovascular disease over 6-year follow-up to assess the risk of incident CHD associated with baseline noninvasive measures of atherosclerosis (ankle-arm index [AAI], aortic pulse wave velocity [aPWV]) and inflammatory markers (interleukin-6 [IL-6], C-reactive protein [CRP], tumor necrosis factor-a [TNF-a]). CHD events were studied as either nonfatal myocardial infarction or coronary death ("hard" events), and "hard" events plus hospitalization for angina, or the need for coronary-revascularization procedures (total CHD events).

Results: During the 6-year follow-up, 283 participants had CHD events (including 136 "hard" events). IL-6, TNF-a and AAI independently predicted CHD events above Framingham Risk Score (FRS) with hazard ratios [HR] for the highest compared as with the lowest quartile for IL-6 of 1.95 (95%CI: 1.38–2.75, p for trend <0.001). TNF-a of 1.45 (95%CI: 1.04–2.02, p for trend 0.03), of 1.96 (95%CI: 1.19–3.21) for AAI <0.9, as compared to AAI 1.01–3.0. CRP and aPWV were not independently associated with CHD events. Results were similar for "hard" CHD events. Addition of IL-6 and AAI to traditional cardiovascular risk factors yielded the greatest improvement in the prediction of CHD: C-index for "hard" total CHD events increased from 0.62/0.62 for traditional risk factors to 0.64/0.64 for IL-6 addition, 0.65/0.63 for AAI, and 0.66/0.64 for IL-6 combined with AAI. Being in the highest quartile of IL-6 combined with an AAI <0.80 or >1.40 yielded an HR of 2.51 (1.50–4.19) and 4.55 (1.65–12.50) above FRS, respectively. With use of CHD risk categories, risk prediction at 5 years was more accurate in models that included IL-6, AAI or both, with 8.0, 8.3 and 12.1% correctly reclassified respectively.

Conclusions: Among older adults, markers of atherosclerosis and of inflammation, especially IL-6 and AAI, are independently associated with CHD events above Framingham Risk Score. These new risk determinants better predict the incidence of CHD above FRS. Addition of IL-6 and AAI to traditional cardiovascular risk factors yields the greatest improvement in the prediction of CHD; C-index for “hard” total CHD events increased from 0.62/0.62 for traditional risk factors to 0.64/0.64 for IL-6 addition, 0.65/0.63 for AAI, and 0.66/0.64 for IL-6 combined with AAI.

Acknowledgments

This study was supported by the National Institute on Aging, NIH.

Carotid Total Plaque Area (TPA): a tool for targeting and evaluating vascular preventive therapy. On behalf of the Taskforce on vascular risk prediction

Romanens M., Dariol R. (Otten, Lausanne)

Since the introduction of TPA in 1992 by Dr David Spenzer and his sonographer Maria DiCocco, two large outcome studies have shown, that TPA has an acceptable power to predict future vascular death, vascular morbidity and mortality, and myocardial infarction. The published data are derived from two studies with >7000 subjects studies and a follow-up of 3 and 6 years, respectively.

TPA is a simple and easily obtained measure of the atherosclerotic burden within both carotid arteries acquired by ultrasound technology. Furthermore, TPA may be used for follow-up examinations in the medical office, in order to guide the intensity of preventive therapies and may be used as a gatekeeper for other atherosclerosis imaging techniques, such as coronary calcium imaging. Comparative data between coronary calcium and TPA have been generated over our laboratory since the year 2002 and allow to give estimates about the TPA diagnostic power to detect high coronary risk scores in the same subject, thereby avoiding risk from irradiation.

Further, different risk prediction models will be discussed with special emphasis on posttest calculations from a real world experience. Finally, a short update on the Taskforce on Vascular Risk Prediction activities will conclude the presentation.

Adult Treatment Panel III metabolic syndrome criteria more strongly than International Diabetes Federation criteria predict the incidence of type 2 diabetes in angiographed coronary patients

Saely C.H., Vonbank A., Rein P., Beer S., Aczel S., Marte T., Drexel H. (Feldkirch)

Background: It is unclear whether the National Cholesterol Education Program (NCEP-ATPIII) criteria, and 204 (40.6%) had the MetS according to IDF criteria. During the follow-up period, T2DM was newly diagnosed in 86 (17.1%) patients. Both definitions of the MetS significantly predicted incident diabetes; however, the adjusted odds ratio was higher for the NCEP-ATPIII MetS (3.55 [2.16–5.86]; p <0.001) than for the IDF MetS (2.19 [1.32–3.43]; p = 0.002). Among the 120 patients (23.9%) in whom the two definitions of the MetS led to discordant diagnoses, the incidence of T2DM was significantly higher in patients who fulfilled the NCEP-ATPIII MetS criteria, but not the IDF criteria than in those who conversely fulfilled the IDF but not the NCEP-ATPIII criteria (33.3% vs. 15.6%; p = 0.051).

Conclusions: We conclude that among angiographed coronary patients, the NCEP-ATPIII criteria of the MetS more strongly than the IDF MetS criteria predict the incidence of T2DM.

Alanine aminotransferase and gamma glutamyl transferase are associated with the metabolic syndrome but not with angiographically determined stable coronary artery disease


Background: Recently, elevated livers enzymes have attracted great interest as potential novel markers of cardiovascular risk. Their association with angiographically determined stable coronary artery disease (CAD) is unknown.

Methods: We enrolled 1000 consecutive patients undergoing coronary angiography for the evaluation of suspected or established stable CAD. The metabolic syndrome (MetS) was defined according to National Cholesterol Education Programme Adult Treatment Panel III criteria; significant CAD was diagnosed in the presence of coronary stenoses with luminal narrowing ≥50%. The incidence of type 2 diabetes (T2DM) was significantly higher in patients with the MetS than in subjects without the MetS (34 ± 21 vs. 29 ± 20 U/l; p <0.001, 1.16 ± 0.39 vs. 1.00 ± 0.36, p <0.001; and 53 ± 88 vs. 43 ± 57 U/l, p = 0.001, respectively). In contrast, these parameters were similar in patients with significant CAD as in those who did not have significant CAD at angiography (p = 0.592; p = 0.731, and p = 0.716, respectively). Analysis of covariance after multivariate adjustment including alcohol consumption confirmed that ALT, ALT/AST ratio, and GGT were significantly and independently associated with the MetS (F = 13.87; p <0.001; F = 19.84; p <0.001; and F = 8.55; p = 0.004, respectively) but not with significant CAD (p = 0.317; p = 0.741, and p = 0.151, respectively).

Conclusions: ALT, the ALT/AST ratio, and GGT are associated with the MetS but not with angiographically determined coronary atherosclerosis. These simple parameters therefore should not be too enthusiastically embraced as novel tools for cardiovascular risk stratification.

Body Mass Index and waist circumference as predictors of the incidence of type 2 diabetes among angiographed coronary patients


Background: No data on the impact of body mass index (BMI) and of waist circumference on the incidence of type 2 diabetes (T2DM) among angiographed coronary patients are available.

Objective: To investigate in as far BMI and waist circumference predict incident T2DM in this clinically important patient population.

Abstracts
High triglycerides, low HDL cholesterol and small LDL particles predict incident type 2 diabetes in non-diabetic coronary patients

Saely C.H., Vonbank A., Rein P., Beer S., Aczel S., Marte T., Dreixel H. (Feldkirch)

Background: Patients with type 2 diabetes mellitus (T2DM) exhibit a typical pattern of dyslipidemia with high triglycerides, low HDL cholesterol, and small LDL particles, which is also frequently observed in pre-diabetic patients. We therefore hypothesized that these lipid abnormalities predict incident T2DM in the high-risk population of angiographed coronary patients.

Methods: The incidence of T2DM was recorded over 6 years in a population of 503 consecutive non-diabetic patients undergoing coronary angiography for the evaluation of stable coronary artery disease.

Results: During follow-up, T2DM was newly diagnosed in 86 (17.1%) of our patients. Impaired fasting glucose (IFG) <100 mg/dl at baseline was present in 53.4% of the study population, and IFG patients were at a significantly higher risk of incident T2DM than patients with normal fasting glucose (24.3% vs. 8.9%; p < 0.001). In logistic regression analysis adjusting for age, gender, BMI, hypertension, and smoking the standardized OR for fasting glucose as a predictor of T2DM was 1.72 [95% CI 1.36–2.18]; p < 0.001 and, in line with our hypothesis, also the serum levels of triglycerides (OR = 1.57 [1.25–1.98]; p < 0.001), HDL cholesterol (OR = 0.62 [0.45–0.86]; p = 0.004) as well as the LDL particle diameter (OR = 0.57 [0.44–0.75]; p < 0.001) proved significantly predictive of incident T2DM. Importantly, triglycerides (OR = 1.49 [1.18–1.88], p = 0.001), HDL cholesterol (OR = 0.66 [0.47–0.91], p = 0.012) and the LDL particle diameter (OR = 0.61 [0.45–0.80], p < 0.001) still significantly predicted T2DM after additional adjustment for the baseline fasting glucose values.

Conclusions: High triglycerides, low HDL cholesterol, and a small LDL particle diameter significantly and independently predict the 6-year incidence of T2DM among non-diabetic coronary patients.

Current cholesterol guidelines and clinical reality: a comparison of coronary artery disease patients from now and from seven years ago

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Background: Current guidelines recommend serum LDL cholesterol <100 mg/dl for patients with stable coronary artery disease (CAD) and <70 mg/dl for the very high risk patients with CAD plus type 2 diabetes (T2DM). We aimed at investigating compliance with these guidelines in two cohorts of CAD patients from now and from seven years ago.

Methods: We obtained lipid panels in two cohorts of patients who were referred to coronary angiography for the evaluation of previously (>1 month) established stable CAD in 1999–2000 (n = 339) and in 2005–2007 (n = 656), respectively.

Results: The prevalence of diabetes was 24.9% in the first and 26.9% in the second cohort. Overall, 59.3% and 64.6% of diabetic patients and 50.8% and 58.5% of non-diabetic patients were on statins in the first and in the second cohort (p for difference between the cohorts = 0.468 and 0.043, respectively). Among non-diabetic patients with CAD, the proportion of subjects with LDL cholesterol <100 mg was 23.5% in the first cohort and 28.3% in the second cohort (p = 0.182); among patients with CAD plus T2DM 36.0% and 40.6% (p = 0.471) and 8.1% and 9.1% (p = 0.788) had LDL cholesterol <100 mg/dl and <70 mg/dl in the first and in the second cohort, respectively.

Conclusion: The proportion of patients with stable CAD who meet current lipid treatment goals is low and has only marginally improved during the last 7 years. This in particular holds true for the very high risk patients with CAD plus diabetes.

The role of ALOX15 in human atherosclerosis and myocardial infarction

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The 15-lipoxygenase (ALOX15) plays a janus-role in inflammation with pro-inflammatory and anti-inflammatory effects in cell cultures and primary cells and even opposite effects on atherosclerosis in two different animal species. To dissect its role in atherosclerosis, we screened the human ALOX15 gene for variations because genetic variability in ALOX15 might influence atherosclerosis and other inflammatory diseases. We detected 11 variations, including five polymorphisms located in the ALOX15 promoter region. One of these polymorphisms, a C to T substitution at position c.-292, created a novel transcription factor binding site for SPI1. SPI1 only bound to the promoter containing c.-292T, which led to three times higher ALOX15 mRNA levels in macrophages from carriers than from non-carriers. To evaluate the influence of the increased transcription on the ALOX15 enzyme activity, we compared the production of the ALOX15 specific metabolite 15-(S)-HETE between 292CT heterozygous volunteers and non-carriers. Primary macrophages from c.-292CT heterozygous volunteers produced 6-times more of the ALOX15 specific product 15-(S)-HETE compared to non-carriers. Intriguingly, this polymorphism showed a tendency to be protective against atherosclerosis in a smaller case-control study for coronary artery disease; however, it was not associated with myocardial infarction in a large case-control study for myocardial infarction. We conclude that ALOX15 may be atheroprotective in early stages of atherosclerosis, however, seems not to be involved during later stages of atherosclerosis involving atherothrombotic mechanisms.