atherosclerosis

Atherosclerosis newsletter

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Lifestyle and effects of concomitant drug use

The genetic set-up of human beings has not changed tremendously over time. However, the risk of atherosclerotic cardiovascular diseases (ASCVD) is altered tremendously during a rather limited period of time. This can be best witnessed in countries which turned a predominantly rural culture into an urban culture. These transitions are accompanied by massive changes in lifestyle, diet, environment, and socioeconomic factors which have a strong impact on disease risks of the individuals and their offspring. In addition, treatment of diseases other than ASCVD has an impact on vascular biology, either directly or indirectly, by affecting risk factors. The May issue Vol 301 contains several articles on the impact of lifestyle factors and concomitant drug treatment on ASCVD and its risk factors.

The relation between healthy lifestyle changes and decrease in systemic inflammation in patients with stable cardiovascular disease

Systemic low-grade inflammation plays a role in the development of atherothrombotic disease by initiating plaque formation and stimulating plaque progression and transformation to vulnerable plaques that are more prone to erosion or rupture. C-reactive protein (CRP), an acute phase protein, is part of the IL-1β, IL-6 inflammatory pathway, and plasma CRP concentrations ≤ 10 mg/L reflect systemic low-grade inflammation. Several medical conditions, as well as lifestyle factors including smoking, abdominal obesity, physical activity, and alcohol intake, influence systemic inflammation. Pharmacological lowering of inflammation has proven effective in reducing recurrent cardiovascular event rates. van't Klooster et al. aimed at evaluating lifestyle changes (smoking cessation, weight loss, physical activity level increase, alcohol moderation, and a summary lifestyle improvement score) in relation to changes in plasma C-reactive protein (CRP) concentration in patients with established cardiovascular disease.

In total, 1794 patients from the Utrecht Cardiovascular Cohort-Second Manifestations of ARTerial disease (UCC-SMART) cohort with stable cardiovascular disease and CRP levels ≤10 mg/L, who returned for a follow-up study visit after a median of 9.9 years, were included. The relation

between changes in smoking status, weight, physical activity, alcohol consumption, a summary lifestyle improvement score and changes in plasma CRP concentration was evaluated with linear regression analyses.

Smoking cessation was related to a 0.40 mg/L decline in CRP concentration. Weight loss and increase in physical activity were related to a decrease in CRP concentration. Change in alcohol consumption was not related to any CRP difference. Every point higher in the summary lifestyle improvement score was related to a decrease in CRP concentration of 0.17 mg/L.

Smoking cessation, increase in physical activity, and weight loss are related to a decrease in CRP concentration in patients with stable cardiovascular disease. Patients with the highest summary lifestyle improvement score have the highest decrease in CRP concentration. These results may indicate that healthy lifestyle changes contribute to lowering systemic inflammation, potentially leading to a lower cardiovascular risk in patients with established cardiovascular disease.

Impact of parental smoking on adipokine profiles and cardiometabolic risk factors in Chinese children

Exposure to second-hand smoke was reported to be an important modifiable factor in addition to unhealthy diet, sedentary lifestyle and insufficient sleep, associated with obesity and cardiometabolic disorders. The mechanisms by which passive smoking leads to cardiometabolic risks, and the tissues involved are now understood. One hypothesis is that the association of second-hand smoke exposure with cardiometabolic risk may be mediated through adiposity, particularly via the adverse effects on the endocrine function of the adipose tissue. Li et al. aimed at evaluating the association of parental smoking exposure (PSE) with the secretion of adipocyte-derived hormones and cardiometabolic risk factors in Chinese children.

3150 school children aged 6-18 years from the Beijing Child and Adolescent Metabolic Syndrome (BCAMS) study were included in the analysis. Data on PSE and potential confounders were collected. Six adipokines related to insulin resistance and metabolic syndrome (MetS) were measured.

PSE was reported in nearly two-thirds of the children. After adjusting for covariates, including age, sex, pubertal stages, lifestyle factors, and family history, PSE was independently associated with increases of 39.2% in leptin and 3.9% in retinol binding protein-4 and decreases of 11.4% in fibroblast growth factor 21 and 4.6% in adiponectin levels, plus risks for central obesity, elevated blood pressure and MetS. However, the associations of PSE with hypertension and MetS were abolished when adjusted for adiposity parameters or the above-mentioned adipokine profiles.

These results suggest that alterations in adipokine levels might mediate the relation between PSE and cardiometabolic disorders in children.

Electronic cigarettes containing nicotine increase endothelial and platelet derived extracellular vesicles in healthy volunteers

Conventional cigarette smoking is attributed to several adverse health effects including respiratory and cardiovascular disease. Following the 2003 patent, electronic cigarettes (e-cigarettes) were launched on a global scale. Whether e-cigarettes are harmful to human health is an intensely debated subject. E-cigarette usage has been linked to various acute adverse physiological changes in humans. These include increased airway inflammation, increased airway obstruction as well as increased levels of endothelial progenitor cells (indicative of vascular changes) and arterial stiffness (an important independent risk factor for future cardiovascular disease). To investigate whether e-cigarettes with and without nicotine cause different vascular responses, Mobarrez et al. measured extracellular vesicles (EVs) of endothelial and platelet origin (as marker of endothelial dysfunction) in blood samples of healthy young volunteers who performed brief active e-cigarette inhalations.

Using a randomized, double-blind, crossover design, 17 healthy occasional smokers inhaled 30 puffs of e-cigarette vapor during 30 min. Blood samples were collected at baseline, 0, 2, 4 and 6 h post-exposure. EVs from platelets and endothelial cells were measured by flow cytometry.

Platelet and endothelial derived EVs were significantly increased, with peak levels at 4 h following exposure to active inhalation of e-cigarette vapor with nicotine. Moreover, platelet derived EVs, expressing the platelet activation marker P-selectin and the inflammation marker CD40 ligand, were also significantly increased following inhalation of e-cigarette vapor with nicotine. In addition, platelet derived EVs expressing CD40 ligand were increased after inhalation of e-cigarette vapor without nicotine.

As few as 30 puffs of nicotine-containing e-cigarette vapor caused an increase in circulating EVs of endothelial and platelet origin, possibly underlying vascular changes. Although e-cigarette vapor without nicotine caused an increase in platelet EVs expressing CD40 ligand, nicotine seems to have a more compelling effect on extracellular vesicle formation and protein composition.

In their editorial, Benedikter and Koenen comment on these observations, highlighting how the EVs released after inhalation of e-cigarette vapor might not only be a biomarker for physiological stress, but also an active propagator of cellular responses promoting vascular and pulmonary inflammation, suggesting that vapor from e-cigarettes might be more similar to regular cigarette smoke than the e-cigarette industry wants to make us believe.

Association of changes in lipids with risk of myocardial infarction among people without lipid-lowering therapy

Although serum lipids are widely accepted as independent predictors of myocardial infarction (MI), there is insufficient evidence for the associations between changes in lipid levels and MI. Tian et al. aimed at investigating the associations between changes in lipids and incidence of MI in people without lipid-lowering therapy.

64,031 Chinese participants without previous MI were enrolled in the study and divided into four categories based on quartiles of lipid changes. Multivariable Cox regression models were used to calculate hazard ratios (HRs) and 95% confidence intervals for MI.

During a median follow-up of 7.03 years, 599 individuals developed MI. After adjustment for covariates, increased total cholesterol (TC), increased low-density lipoprotein cholesterol (LDL-C), increased non-high-density lipoprotein cholesterol (non-HDL-C), and decreased high-density lipoprotein cholesterol (HDL-C) were associated with elevated risk of MI, with HRs in the highest quartile group compared with the lowest quartile group of 1.56, 1.96, 1.95, and 0.69, respectively. However, changes in triglyceride (TG) were not associated with MI risk.

Changes in levels of TC, LDL-C, non-HDL-C, and HDL-C, but not TG, were associated with risk of MI. Early detection and control of lipid levels may be beneficial and necessary for young people and those with healthy lipid levels at baseline.

Association between the cumulative exposure to bisphosphonates and hospitalization for atherosclerotic cardiovascular events: A population-based study

Cardiovascular disease (CVD) and osteoporosis are common age-related conditions. They are both associated with increased morbidity and mortality, and their socioeconomic and health care impact is considerable. Bisphosphonates are widely used in clinical practice to prevent and treat osteoporosis. Experimental studies suggest that bisphosphonates interfere with the arterial calcification process and inhibit atherosclerosis and vascular calcification. Epidemiologic studies have reported a lower risk of myocardial infarction or stroke among bisphosphonate users compared with non-users. Although bisphosphonates have been suggested to protect against atherosclerotic cardiovascular (CV) events, evidence is still conflicting. Casula et al. aimed at investigating the effect of bisphosphonates on hospitalizations for atherosclerotic CV events.

A retrospective cohort study selecting subjects aged>40 years, incident users of bisphosphonates was carried out. Exposure to bisphosphonates was characterized based on cumulative doses (proportion of days covered, PDC). Treatment's adherence was classified as low (PDC≤40%), intermediate (PDC 41%–80%), or high (PDC>80%). A multivariate Cox model was fitted to

estimate the association between cumulative time-dependent exposure to bisphosphonates and hospitalization for atherosclerotic CV events.

Among 82,704 new bisphosphonates users, 16.1% had a CV hospitalization during a mean follow-up of 6.5 + 2.6 years. Compared with individuals with PDC ≤40%, those exposed for 41–80% or more than 80% showed HRs of CV hospitalization of 0.95 and 0.75, respectively. In the sub-analysis by type of event, a PDC >80% was associated with a reduced incidence for both coronary and cerebrovascular events. The protective effect was confirmed in stratified analyses by sex and age classes, and in those performed at 1 and 3 years of follow-up.

Strict adherence to bisphosphonate treatment was associated with a better CV outcome. Although further studies to investigate possible mechanisms are warranted, bisphosphonates could be considered as having a potential CV benefit beyond the effect on bones.