[1] *Hussain S, Golozar A, Widney DP et al.* **Effect of statin use on inflammation and immune activation biomarkers in HIV-infected persons on effective anti-retroviral therapy**. AIDS research and human retroviruses 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33238713
ABSTRACT
BACKGROUND: Immune activation and inflammation are hallmarks of chronic HIV infection and are etiologically linked to major causes of morbidity and mortality among HIV-infected persons, including coronary artery disease and cancer. Systemic immune activation is dampened, but not resolved, with use of combination antiretroviral therapy (cART). Statins are cardioprotective drugs that also appear to have immunomodulatory and anti-inflammatory properties. We sought to understand the association between statin use, cART, and levels of circulating immune markers in a longitudinal cohort study. METHODS: From 2004-2009, statin use was ascertained in male participants of the Multicenter AIDS Cohort Study (MACS) using interviewer-administered questionnaires. Twenty-four circulating markers of immune activation and inflammation were measured in archived serial samples from a subset of cohort members using multiplex assays. Propensity-adjusted generalized gamma models were used to compare biomarkers' distributions by statin use, and multivariable linear regression models were used to assess the effect of initiating statin on these biomarkers. RESULTS: Overall, 1,031 cART-exposed individuals with HIV infection were included in this study. Statin use was reported by 31.5% of cART-exposed participants. Compared to non-statin users on cART, statin users on cART had lower levels of IP-10, IL-10 and IL-12p70, and the effect of statin use was decreased in participants using lipophilic statins (atorvastatin, simvastatin, fluvastatin, or lovastatin); these results were statistically significant ($p<0.05$). Among cART users not on aspirin, starting statins decreased levels of hsCRP, IL-12p70, and IL-6. CONCLUSION: Statin therapy is associated with reduced levels of certain biomarkers of immune activation and inflammation in cART users, which may contribute to a lower burden of disease.

[2] *Karapostolakis G, Vakaki M, Attilakos A et al.* **The Effect of Long-Term Atorvastatin Therapy on Carotid Intima-Media Thickness of Children With Dyslipidemia**. Angiology 2020:3319720975635.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33242982
ABSTRACT
Carotid intima-media thickness (cIMT) has been proposed as an early marker of subclinical atherosclerosis in high risk children. Children with heterozygous familial hypercholesterolemia have greater cIMT than matched healthy controls or their unaffected siblings. Statin therapy may delay the progression of cIMT, although long-term studies in children are scarce. We evaluated the effect of atorvastatin treatment on cIMT in children with dyslipidemia. We studied 81 children/adolescents, 27 with severe dyslipidemia (low-density lipoprotein cholesterol [LDL-C] ≥190 mg/dL) and 54 sex- and age-matched healthy controls; LDL-C ≤ 130 mg/dL and lipoprotein (a), Lp(a), ≤30 mg/dL. In the children with dyslipidemia, cIMT was measured twice, before and on treatment (18.2 ± 7.7 months). Anthropometric data, a full lipid profile, liver, kidney, and thyroid function were evaluated. Males with dyslipidemia had a greater cIMT than male controls after adjustment for other factors (P = .049). In addition, a nonstatistically significant decrease in cIMT was observed after treatment (P = .261). Treatment with atorvastatin resulted in a significantly improved lipid profile. Females with dyslipidemia had a significantly thinner cIMT than males. Children with normal and high Lp(a) levels had similar

cIMT values. In conclusion, treatment with atorvastatin had a beneficial effect on the lipid profile and cIMT progression in children with severe dyslipidemia.

[3] *Musunuru K*. **Treating Coronary Artery Disease: Beyond Statins, Ezetimibe, and PCSK9 Inhibition**. Annual review of medicine 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33234004
ABSTRACT
Statins, ezetimibe, and PCSK9 inhibitors are currently the standard of care for the prevention and treatment of coronary artery disease. Despite their widespread use, coronary artery disease remains the leading cause of death worldwide, a fact that pleads for the development of new protective therapies. In no small part due to advances in the field of human genetics, many new therapies targeting various lipid traits or inflammation have recently received approval from regulatory agencies such as the US Food and Drug and Administration or fared favorably in clinical trials. This wave of new therapies promises to transform the care of patients at risk for life-threatening coronary events. Expected final online publication date for the Annual Review of Medicine, Volume 72 is January 27, 2021. Please see http://www.annualreviews.org/page/journal/pubdates for revised estimates.

[4] *Shakour N, Ruscica M, Hadizadeh F et al.* **Statins and C-reactive protein: in silico evidence on direct interaction**. Archives of medical science : AMS 2020; 16:1432-1439.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33224343
ABSTRACT
INTRODUCTION: Statins are known to lower CRP, and this reduction has been suggested to contribute to the established efficacy of these drugs in reducing cardiovascular events and outcomes. However, the exact mechanism underlying the CRP-lowering effect of statins remains elusive. METHODS: In order to test the possibility of direct interaction, we performed an in silico study by testing the orientation of the respective ligands (statins) and phosphorylcholine (the standard ligand of CRP) in the CRP active site using Molecular Operating Environment (MOE) software. RESULTS: Docking experiments showed that all statins could directly interact with CRP. Among statins, rosuvastatin had the strongest interaction with CRP (pKi = 16.14), followed by fluvastatin (pKi = 15.58), pitavastatin (pKi = 15.26), atorvastatin (pKi = 14.68), pravastatin (pKi = 13.95), simvastatin (pKi = 7.98) and lovastatin (pKi = 7.10). According to the above-mentioned results, rosuvastatin, fluvastatin, pitavastatin and atorvastatin were found to have stronger binding to CRP compared with the standard ligand phosphocholine (pKi = 14.55). CONCLUSIONS: This finding suggests a new mechanism of interaction between statins and CRP that could be independent of the putative cholesterol-lowering activity of statins.

[5] *Reeskamp LF, Tromp TR, Huijgen R et al.* **Statin therapy reduces plasma angiopoietin-like 3 (ANGPTL3) concentrations in hypercholesterolemic patients via reduced liver X receptor (LXR) activation**. Atherosclerosis 2020; 315:68-75.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33242792
ABSTRACT
BACKGROUND AND AIMS: Statins suppress hepatic mRNA expression of ANGPTL3 encoding angiopoietin-like 3 in healthy subjects, but it is unknown if plasma ANGPTL3 concentrations are affected by statins prescribed to hypercholesterolemic patients in clinical practice. We therefore

investigated the effect of statin treatment on plasma ANGPTL3 concentrations in hypercholesterolemic patients. In addition, we explored the underlying mechanism by which statins regulate ANGPTL3 in vitro. METHODS: Plasma ANGPTL3 concentrations were measured in 93 genetically confirmed familial hypercholesterolemia (FH) patients who were using statin therapy and 61 statin naïve FH patients. Moreover, concentrations were measured in 14 hypercholesterolemic patients who discontinued their statin treatment for 4 weeks. In vitro studies were performed with Huh7 human hepatoma cells. RESULTS: Plasma ANGPTL3 concentrations were 15% lower in statin treated FH patients compared to statin naïve FH patients (145 (120-193) vs. 167 (135-220) ng/ml, p = 0.012). Statin discontinuation resulted in a 21% (p<0.001) increase of plasma ANGPTL3 concentrations. Simvastatin reduced ANGPTL3 mRNA expression and ANGPTL3 secretion of Huh7 cells. Liver X receptor (LXR) activation with T0901317 increased ANGPTL3 mRNA expression and ANGPTL3 secretion by 6- and 3-fold, respectively. Adding simvastatin did not mitigate this effect but adding the LXR antagonist GSK2230 to simvastatin-incubated Huh7 cells diminished simvastatin-induced reductions in ANGPTL3 mRNA expression and ANGPTL3 secretion. Simvastatin reduced intracellular oxysterol concentrations. Oxysterols are endogenous LXR ligands, implying that simvastatin suppresses ANGPTL3 secretion via reduced oxysterol-mediated LXR activation. CONCLUSIONS: Statins lower plasma ANGPTL3 concentrations in hypercholesterolemic patients, likely due to decreased oxysterol-mediated LXR activation.

[6] *Kris-Etherton PM, Petersen K, Van Horn L*. **Convincing evidence supports reducing saturated fat to decrease cardiovascular disease risk**. BMJ Nutr Prev Health 2018; 1:23-26.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33245724
ABSTRACT

[7] *Pot GK, Battjes-Fries MC, Patijn ON et al.* **Nutrition and lifestyle intervention in type 2 diabetes: pilot study in the Netherlands showing improved glucose control and reduction in glucose lowering medication**. BMJ Nutr Prev Health 2019; 2:43-50.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33235957
ABSTRACT
INTRODUCTION: Prevalence of type 2 diabetes (T2D) is increasing rapidly and lifestyle interventions to reverse diabetes are seen as a possible solution to stop this trend. New practice-based evidence is needed to gain more insight in the actual, and above all scientific, basis for these claims. METHODS: This observational study with a pretest post-test design aimed to pilot a 6-month multicomponent outpatient group-based nutrition and lifestyle intervention programme on glycaemic control and use of glucose lowering medication in motivated T2D patients with a body mass index (BMI) >25 kg/m(2) in the Netherlands (February 2015-March 2016). RESULTS: 74 T2D patients (56% female) aged 57.4±8.0 years with mean BMI 31.2±4.2 kg/m(2) and mean waist circumference 105.4±10.2 cm were included in the study. Compared with baseline, mean HbA1c levels at 6 months were 5 mmol/mol lower (SD=10, p<0.001) and the number of participants with HbA1c levels ≤53 mmol/mol after intervention had increased (from 36% (n=26/72) to 60% (n=43/72)). At baseline, 90% of participants were taking at least one type of glucose lowering medication. At 6 months, 49% (n=35/72) of the participants had reduced their medication or eliminated it completely (13%). Secondary outcomes were significantly lower fasting glucose levels (- 1.2±2.6 mmol/L), body weight (-4.9±5.1 kg), BMI (-1.70±1.69 kg/m(2)) and waist circumference (-9.4±5.0 cm). Plasma lipids remained unchanged except

for a decrease in triglyceride levels. Furthermore, self-reported quality of life was significantly higher while experienced fatigue and sleep problems were significantly lower. CONCLUSION: This pilot study showed that a 6-month multicomponent group-based program in a routine care setting could improve glycaemic control and reduce the use of glucose lowering medication in motivated T2D diabetics. A fully scaled study is needed to confirm these results.

[8] *Pase CS, Metz VG, Roversi K et al.* **Trans fat intake during pregnancy or lactation increases anxiety-like behavior and alters proinflammatory cytokines and glucocorticoid receptor levels in the hippocampus of adult offspring**. Brain research bulletin 2021; 166:110-117.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33242520

ABSTRACT

Changes in dietary habits, including the increased consumption of processed foods, rich in trans fatty acids (TFA), have profound effects on offspring health in later life. Thus, this study aimed to assess the influence of maternal trans fat intake during pregnancy or lactation on anxiety behavior, as well as markers of inflammation, oxidative stress, and expression of glucocorticoid receptors (GR) of adult male offspring. Female Wistar rats were supplemented daily with soybean oil/fish oil (SO/FO) or hydrogenated vegetable fat (HVF) by oral gavage (3.0 g/kg body weight) during pregnancy or lactation. After weaning, male offspring received only standard diet. On the postnatal day 60, anxiety-like symptoms were assessed, the plasma was collected for the quantification of cytokines levels and the hippocampus removed for biochemical and molecular analysis. Our findings have evidenced that offspring from HVF-supplemented dams during pregnancy or lactation showed significantly greater levels of anxiety behavior. HVF supplementation increased plasma levels of proinflammatory cytokines and these levels were higher in the lactation period. In contrast, HVF supplementation decreased plasma levels of IL-10 in relation to SO/FO in both periods. Biochemical evaluations showed higher reactive species generation, protein carbonyl levels and catalase activity in offspring from HVF-supplemented dams during lactation. In addition, offspring from HVF-supplemented dams showed decreased GR expression in both supplemented periods. Together, these data indicate that consumption of TFA in different periods of development may increase anxiety-like behavior at least in part via alterations in proinflammatory and anti-inflammatory cytokine levels and GR expression in limbic brain regions.

[9] *Montarello NJ, Nelson AJ, Verjans J et al.* **The role of intracoronary imaging in translational research**. Cardiovascular diagnosis and therapy 2020; 10:1480-1507.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33224769

ABSTRACT

Atherosclerotic cardiovascular disease is a key public health concern worldwide and leading cause of morbidity, mortality and health economic costs. Understanding atherosclerotic plaque microstructure in relation to molecular mechanisms that underpin its initiation and progression is needed to provide the best chance of combating this disease. Evolving vessel wall-based, endovascular coronary imaging modalities, including intravascular ultrasound (IVUS), optical coherence tomography (OCT) and near-infrared spectroscopy (NIRS), used in isolation or as hybrid modalities, have been advanced to allow comprehensive visualization of the pathological substrate of coronary atherosclerosis and accurately measure temporal changes in both the vessel wall and plaque characteristics. This has helped further our appreciation of the natural history of coronary artery

disease (CAD) and the risk for major adverse cardiovascular events (MACE), evaluate the responsiveness to conventional and experimental therapeutic interventions, and assist in guiding percutaneous coronary intervention (PCI). Here we review the use of different imaging modalities for these purposes and the lessons they have provided thus far.

[10] *Egbaria A, Saliba W, Zafrir B*. **Assessment of Low LDL Cholesterol in Patients Treated by PCSK9 Inhibition: Comparison of Martin/Hopkins and Friedewald Estimations**. Cardiovascular drugs and therapy / sponsored by the International Society of Cardiovascular Pharmacotherapy 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33226544

ABSTRACT

PURPOSE: Recent guidelines recommend further reduction of low-density lipoprotein cholesterol (LDL-C) in high-risk populations. The use of proprotein convertase subtilisin/kexin type-9 inhibitors (PCSK9i) enables many patients to achieve profound reduction in LDL-C. However, in patients with low cholesterol, the commonly used Friedewald equation tends to underestimate LDL-C, which may result in undertreatment. We aimed to compare Friedewald LDL-C estimation with the more novel Martin/Hopkins method in PCSK9i-treated patients achieving low LDL-C. METHODS: We investigated high-risk patients treated by PCSK9i in whom Friedewald LDL-C levels were <70 mg/dL and triglycerides ≤300 mg/dL. LDL-C was additionally assessed by the Martin/Hopkins method. The compatibility between estimations was evaluated using methods of concordance and reclassification between LDL-C categories (<25, 25-40, 40-55, 55-70 mg/dL) and according to triglyceride strata. RESULTS: Mean age was 65 ± 10 years. The correlation coefficient between LDL-C estimations was r = 0.898. Martin/Hopkins reclassified 269 of the 608 patients (44%) to a higher LDL-C category, with 14% of the patients reaching LDL-C >70 mg/dL. Of the 390 patients achieving Friedewald LDL-C <55 mg/dL, 113 (29%) were estimated to have LDL-C ≥55 mg/dL by the Martin/Hopkins equation. The magnitude of discordance between LDL-C estimates was more pronounced in hypertriglyceridemic patients in whom LDL-C reclassification from <55 to ≥55 mg/dL was observed in 48%. CONCLUSIONS: In real-world practice of high-risk patients achieving low LDL-C under PCSK9i, Martin/Hopkins algorithm displayed significant proportion of LDL-C upward discordance compared to the Friedewald equation, particularly observed in patients with elevated triglycerides, identifying patients that may need treatment intensification.

[11] *Nashawi M, Sheikh O, Mir M et al.* **The systemic implication of novel non-statin therapies in cardiovascular diabetology: PCSK9 as a case model**. Cardiovascular endocrinology & metabolism 2020; 9:143-152.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33225229

ABSTRACT

PCSK9, like other novel non-statin drugs were primarily developed to help patients achieve low-density lipoprotein cholesterol targets, especially in patients with dyslipidemia not achieving lipid goals with statins due to poor tolerance or inadequate response. PCSK9 inhibitors, in addition to modulating lipid metabolism, improve mortality outcomes in cardiovascular disease. These benefits are markedly pronounced in patients with type 2 diabetes mellitus. However, these benefits do not come without associated risk. Multiple trials, studies, and case reports have attempted to explain observed outcomes with PCSK9 expression and administration of PCSK9 inhibitors from multiple perspectives, such as their effects on insulin sensitivity and glucose tolerance, changes in renal

physiology, thyroid physiology, vascular tone, intestinal regulation of lipids, and improved cardiovascular function. These agents represent an opportunity for physicians to exercise prudence by using appropriate clinical judgement when managing comorbidities in the hyperglycemic patient, a concept that extends to other novel non-statin drugs.

[12] *Song K, Park G, Choi Y et al.* **Association of Vitamin D Status and Physical Activity with Lipid Profile in Korean Children and Adolescents: A Population-Based Study**. Children (Basel) 2020; 7.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33228115
ABSTRACT
Dyslipidemia is one of the important influencing factors of cardiovascular health in the youth, and thus, assessment of its etiology is important. We aimed to investigate the association of dyslipidemia with vitamin D and physical activity in Korean children and adolescents. Data of 3183 subjects aged 12-18 years in the Korea National Health and Nutrition Examination Survey were analyzed. Participants were divided into subgroups according to sex, body mass index, 25-hydroxyvitamin D levels, and lipid profile. The mean 25-hydroxyvitamin D level was 16.15 ng/mL, which was below normal. In total, 79.3% of the subjects had vitamin D deficiency. Females had lower vitamin D levels and a higher incidence of dyslipidemia compared to males. Vitamin D deficiency was significantly associated with high density lipoprotein cholesterol (HDL-C) levels. The low HDL-C group consisted of a higher proportion of subjects with vitamin D deficiency and low physical activity. This study suggests that vitamin D deficiency is prevalent in Korean children and adolescents. Vitamin D deficiency and low physical activity are related with low HDL-C levels. Maintaining sufficient vitamin D levels and physical activity may help prevent dyslipidemia.

[13] *Trinder M, Wang Y, Madsen CM et al.* **Inhibition of Cholesteryl Ester Transfer Protein Preserves High-Density Lipoprotein Cholesterol and Improves Survival in Sepsis**. Circulation 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33228395
ABSTRACT
Background: The high-density lipoprotein (HDL) hypothesis of atherosclerosis has been challenged by clinical trials of cholesteryl ester transfer protein (CETP) inhibitors which failed to show significant reductions in cardiovascular events. Plasma levels of HDL-cholesterol (HDL-C) decline drastically during sepsis and this phenomenon is explained, in part, by the activity of CETP, a major determinant of plasma HDL-C levels. We tested the hypothesis that genetic or pharmacologic inhibition of CETP would preserve HDL levels and decrease mortality in clinical cohorts and animal models of sepsis. Methods: We examined the effect of a gain-of-function variant in CETP (rs1800777, p.Arg468Gln) and a genetic score for decreased CETP function on 28-day sepsis survival using Cox proportional hazard models adjusted for age and sex in the UK Biobank (n=5,949), Identification of SNPs Predisposing to Altered Acute Lung Injury Risk (iSPAAR; n=882), Copenhagen General Population Study (n=2,068), Copenhagen City Heart Study (n=493), Early Infection (n=200), St. Paul's Intensive Care Unit 2 (n=203), and Vasopressin versus Norepinephrine Infusion in Patients with Septic Shock studies (n=632). We then studied the effect of the CETP inhibitor anacetrapib in adult, female APOE*3-Leiden mice with or with human CETP expression using the cecal-ligation and puncture model of sepsis. Results: A fixed-effect meta-analysis of all 7 cohorts found that the CETP gain-of-

function variant was significantly associated with increased risk of acute sepsis mortality (hazard ratio [95% confidence interval]: 1.44 [1.22-1.70], p<0.0001). In addition, a genetic score for decreased CETP function was associated with significantly decreased sepsis mortality in the UK Biobank (hazard ratio [95% confidence interval]: 0.77 [0.59-1.00] per 1 mmol/L increase in HDL-C) and iSPAAR cohorts (hazard ratio [95% confidence interval]: 0.60 [0.37-0.98] per 1 mmol/L increase HDL-C). APOE*3-Leiden.CETP mice treated with anacetrapib had preserved levels of HDL-C and apolipoprotein-AI and increased survival relative to placebo treatment (70.6% vs 35.3%, Log-rank p=0.03), while there was no effect of anacetrapib on the survival of APOE*3-Leiden mice which do not express CETP (50.0% vs 42.9%, Log-rank p=0.87). Conclusions: Clinical genetics and humanized mouse models suggest that inhibiting CETP may preserve HDL levels and improve outcomes for individuals with sepsis.

[14] *Schimmenti C, Sucato V, Manzone E et al.* **Bempedoic acid as adjunct for traditional lipid-lowering therapy in patients with hyperlipidaemia**. Coronary artery disease 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33229935
ABSTRACT
Statin therapy has been the cornerstone for the reduction of cholesterol and circulating low-density lipoprotein (LDL) in patients with cardiovascular diseases. However, statin monotherapy has disadvantages attributable to myopathies and to the insufficient cholesterol reduction observed in some patients. There is a need for new well-tolerated therapies for lowering LDL. This review will focus on bempedoic acid in combination with traditional statin therapy or other lipid-lowering agents and its emerging role in LDL-C lowering. Bempedoic acid is also a viable alternative for reducing LDL cholesterol in the treatment of some patients suffering from heterozygous familial hypercholesterolemia.

[15] *Sousa AA, Renke G, Leal A, Jr. et al.* **Current evidence regarding Low-carb diets for the metabolic control of type-2 diabetes**. Current diabetes reviews 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33231159
ABSTRACT
The management of diabetes requires a medical nutritional therapy as an essential part of this treatment. There should be no 'one-size-fits-all' eating pattern for different patient´s profiles with diabetes. It´s clinically complex to suggest an ideal percentage of calories from carbohydrates, protein and lipids recommended for all patients with diabetes. Among the eating patterns that have shown beneficial effects on metabolic control of patients with type 2 diabetes is the Low-Carb diet, since the carbohydrate ingestion is viewed as the most important determinant of postprandial glucose and insulin response. In this context, theoretically it could make sense to reduce the daily amount of carbohydrates ingested, willing to achieve lower levels of HbA1c. There could be associated risks to this approach. The adherence to a Low-Carb Diet is here also discussed. This narrative review works on the current evidence for answering these questions regarding Low-Carb Diet as a possible alternative eating pattern for type 2 diabetes.

[16] *Jayakumari C, Jabbar PK, Soumya S et al.* **Lipid Profile in Indian Patients With Type 2 Diabetes: The Scope for Atherosclerotic Cardiovascular Disease Risk Reduction**. Diabetes spectrum : a publication of the American Diabetes Association 2020; 33:299-306.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33223767

ABSTRACT

OBJECTIVE: Reduction of atherosclerotic cardiovascular disease (ASCVD) risk in patients with diabetes requires proper management of lipid parameters. This study aimed to find the pattern of dyslipidemia and scope of ASCVD risk reduction in patients with diabetes by lipid management. METHODS: Clinical, biochemical, and medication profiles of all patients with diabetes attending a tertiary diabetes care hospital over a 2-year period were collected. The prevalence of various lipid abnormalities was determined after excluding patients with thyroid dysfunction and those on lipid-lowering medications. Patients were stratified according to LDL cholesterol, HDL cholesterol, and triglyceride levels, and other clinical parameters were compared among the groups. The adequacy of statin treatment was assessed based on American Diabetes Association guidelines. RESULTS: Nine hundred and seventy-one patients were included. The prevalence of hyperlipidemia was 40.0%, of whom 14.6% were newly diagnosed. The most common lipid abnormality was elevated LDL cholesterol. Higher A1C and fasting blood glucose values were found to be associated with higher LDL cholesterol levels. Twenty-seven percent of patients with indications for treatment with statins were receiving them. Of those being treated with statins, 42.6% had an LDL cholesterol level ≥100 mg/dL. CONCLUSION: In South Indian patients with type 2 diabetes and fair glycemic control, high LDL cholesterol is the predominant lipid abnormality. There remains a huge potential for ASCVD risk reduction in this population if the knowledge practice gap is addressed.

[17] *Rhee MY, Kim CH, Ahn Y et al.* **Efficacy and Safety of Nebivolol and Rosuvastatin Combination Treatment in Patients with Concomitant Hypertension and Hyperlipidemia**. Drug design, development and therapy 2020; 14:5005-5017.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33235439

ABSTRACT

PURPOSE: We evaluated the efficacy and safety of nebivolol and rosuvastatin combination treatment in patients with hypertension and hyperlipidemia. PATIENTS AND METHODS: Eligible patients, after more than 4 weeks of therapeutic lifestyle change, were randomly assigned to three groups: 5 mg nebivolol plus 20 mg rosuvastatin (NEBI/RSV), 20 mg rosuvastatin (RSV), or 5 mg nebivolol (NEBI). Treatments lasted 8 weeks. RESULTS: Efficacy was analyzed using data from 276 patients. Sitting systolic and diastolic blood pressures differed between the NEBI/RSV and RSV groups (LSmean difference = -5.89 and -5.99 mmHg; 95% confidence interval [CI] = -9.88 to -1.90 mmHg and -8.13 to -3.84 mmHg, respectively). Reductions in the two pressures did not differ between the NEB/RSV and NEB groups. The percent reduction in low-density lipoprotein (LDL) cholesterol differed between the NEBI/RSV and NEBI groups (LSmean difference = -47.76%, 95% CI = -52.69 to -42.84%) but not between the NEBI/RSV and RSV groups. The blood pressure (BP) control rate was higher in the NEBI/RSV group than in the RVS group (51.09% vs 29.67%, $p = 0.003$). The LDL cholesterol goal achievement rate was higher in the NEBI/RSV group than in the NEBI group (85.87% vs 11.83%, $p < 0.001$). The incidence of adverse drug reactions in the NEBI/RSV, RSV, and NEBI groups was 8.51%, 7.45%, and 8.60%, respectively ($p = 0.950$). CONCLUSION: Nebivolol plus rosuvastatin treatment is effective in reducing BP and LDL cholesterol levels and is safe in patients with hypertension and hypercholesterolemia without the loss of BP or the LDL cholesterol-lowering effect of each drug. TRIAL REGISTRATION: CRIS registration number KCT0002148.

[18] *Kutoh E, Kuto AN, Wada A et al.* **Sitagliptin as an Initial Therapy and Differential Regulations of Metabolic Parameters Depending on its Glycemic Response in Subjects with Type 2 Diabetes**. Drug research 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33241550
ABSTRACT
The aim of this study is to investigate whether sitagliptin can be used as an initial drug for T2DM and to evaluate its effects on metabolic parameters in relation to its glycemic efficacies. The subjects received 25-50 mg/day sitagliptin monotherapy (n=69). At 3 months, they were divided into three groups (n=23 each) according to the novel parameter called "A1c index" which is designed to assess glycemic efficacy. The metabolic parameters were compared between good-responders and poor-responders. These two groups acted as a control each other. In the overall subjects, efficient reductions of HbA1c (10.16-8.22%) were observed with few adverse events. Significant correlations were seen between the A1c index and changes of (Δ)nonHDL-C (R=0.250) or ΔLDL-C (R=0.368). At baseline, T-C, nonHDL-C and BMI levels were significantly lower in good-responders than poor-responders. At 3 months, in good-responders, HbA1c levels effectively decreased (11.03-7.00%). Indexes for insulin sensitivity/resistance [HOMA-R and 20/(C-peptide x FBG)] and beta-cell function (HOMA-B and CPR-index) ameliorated. T-C, nonHDL-C and LDL-C significantly decreased, while BMI increased. However, in poor-responders, no changes in these parameters were noted. Collectively, these results suggest that 1) Sitagliptin can be used as a first-line drug for T2DM and its glycemic efficacy is linked to some atherogenic lipids. 2) Those with lower T-C, nonHDL-C and BMI appear to respond better with this drug. 3) Good glycemic efficacy of sitagliptin is medicated through reduced insulin resistance as well as enhanced beta-cell functions. Body weight increased, while some atherogenic cholesterol decreased in good-responders.

[19] *Ruscica M, Greco MF, Ferri N, Corsini A*. **Lipoprotein(a) and PCSK9 inhibition: clinical evidence**. European heart journal supplements : journal of the European Society of Cardiology 2020; 22:L53-l56.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33239979
ABSTRACT
Compelling evidence has emerged from epidemiological and Mendelian randomization analyses relative to the causality of lipoprotein(a) [Lp(a)] in atherosclerotic cardiovascular diseases (ASCVD), being elevated Lp(a) a strong risk factor regardless of the reduction of LDL-C achieved by statins. So far, no specific available agent can lower Lp(a) to the extent required to achieve a cardiovascular (CV) benefit, i.e. approximately 100 mg/dL. The most recent outcomes trial FOURIER with evolocumab showed that a 25 nmol/L (12 mg/dL) reduction in Lp(a) corresponded to a 15% decrement in the relative risk of cardiovascular disease. The ODYSSEY OUTCOMES trial with alirocumab has been the first demonstrating that a reduction in Lp(a) associates with less major adverse cardiovascular events (MACE), i.e. hazard ratio: 0.994 per 1 mg/dL decrement in Lp(a). The Lp(a) lowering effect driven by PCSK9 inhibition was confirmed in carriers of PCSK9 loss-of-function mutations in which Lp(a) and oxPL-apoB levels were decreased compared to non-carriers as was for a slight larger number of apo(a) Kringle IV repeats. Although PCSK9 inhibitors are not able to decrease Lp(a) to the extent required to achieve a CV benefit, their use has led to a higher discontinuation rate in lipoprotein apheresis in patients with progressive ASCVD and high plasma Lp(a).

[20] *Boyle EC, Haverich A*. **Microvasculature dysfunction as the common thread between atherosclerosis, Kawasaki disease, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-associated multi-system inflammatory syndrome in children**. Eur J Cardiothorac Surg 2020; 58:1109-1110.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33247736
ABSTRACT

[21] *Ragusa R, Basta G, Neglia D et al.* **PCSK9 and atherosclerosis: Looking beyond LDL regulation**. European journal of clinical investigation 2020:e13459.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33236356
ABSTRACT
Proprotein Convertase Subtilisin/Kexin type 9 (PCSK9) is involved in cholesterol homeostasis. After binding to the complex low-density lipoprotein (LDL)-receptor, PCSK9 induces its intracellular degradation, thus reducing serum LDL clearance. In addition to the well-known activity on the hepatic LDL receptor-mediated pathway, PCSK9 has been, however, associated with vascular inflammation in atherogenesis. Indeed, PCSK9 is expressed by various cell types that are involved in atherosclerosis (e.g. endothelial cells, smooth muscle cells and macrophages) and is detected inside human atherosclerotic plaques. We here analyse the biology of PCSK9 and its possible involvement in molecular processes involved in atherosclerosis, beyond the regulation of circulating LDL cholesterol levels.

[22] *Yagi T, Ataka K, Cheng KC et al.* **Red rice koji extract alleviates hyperglycemia by increasing glucose uptake and glucose transporter type 4 levels in skeletal muscle in two diabetic mouse models**. Food & nutrition research 2020; 64.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33240034
ABSTRACT
BACKGROUND: Red rice koji (RRK), prepared by growing Monascus species on steamed rice, has been reported to lower blood glucose levels in diabetic animal models. However, the action mechanism is not yet completely understood. OBJECTIVE: The objective of this study was to examine the mechanism underlying the hypoglycemic action of RRK extract in two diabetic animal models: the insulin-deficiency mice, where the insulin deficiency was induced by streptozotocin (STZ), and insulin-resistance mice, where the insulin resistance was induced by a high-fat diet (HFD). DESIGN: Low (12.5 mg/kg body weight [BW]) and high (50.0 mg/kg BW) doses of RRK extract were orally administered to the mice for 10 successive days (0.25 mL/day/mouse). The protein expression levels of glucose transporter type 4 (GLUT4) in the skeletal muscle and glucose transporter type 2 (GLUT2) in the liver were measured. Blood glucose (BG) levels of STZ-treated mice in insulin tolerance test (ITT) and BG and insulin levels of HFD-fed mice in intraperitoneal glucose tolerance test (IPGTT) were investigated. RESULTS: In the STZ-treated mice, oral administration of RRK extract lowered BG levels and food intake but increased plasma 1,5-anhydroglucitol level. Moreover, the RRK extract lowered the BG levels of STZ-treated mice as measured by ITT. In the HFD-fed mice, we confirmed that the orally administered RRK extract lowered the BG and the homeostasis model assessment index for insulin resistance. Furthermore, the RRK extract lowered the BG and insulin levels of HFD-fed mice in IPGTT. Regarding the protein levels of GLUT, the orally

administered RRK extract increased the GLUT4 level in the skeletal muscle; however, the RRK extract did not alter the GLUT2 level in the liver of either the STZ-treated or the HFD-fed mice. DISCUSSION: Our study demonstrates that RRK extract can improve impaired glucose tolerance in mouse models of diabetes by enhancing GLUT4 expression in skeletal muscle. CONCLUSION: These results suggest that RRK extract could potentially be a functional food for the treatment of diabetes mellitus.

[23] *Li YY, Wang H, Yang XX et al.* **PCSK9 Gene E670G Polymorphism and Coronary Artery Disease: An Updated Meta-Analysis of 5,484 Subjects**. Frontiers in cardiovascular medicine 2020; 7:582865.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33244470

ABSTRACT

Objective: Research has shown a possible relationship between the E670G polymorphism of the proprotein convertase subtilisin/kexin type 9 (PCSK9) gene and an increased risk of coronary artery disease (CAD). However, there is no clear consensus on the subject because of conflicting results in the literature. The current meta-analysis was performed to better elucidate the potential relationship between the PCSK9 gene E670G polymorphism and CAD. Methods: There were 5,484 subjects from 13 individual studies who were included in the current meta-analysis. The fixed- or random-effects models were used to evaluate the pooled odds ratios (ORs) and their corresponding 95% confidence intervals (CIs). Results: The current meta-analysis found a significant association between PCSK9 gene E670G polymorphism and CAD under allelic (OR = 1.79, 95% CI = 1.42-2.27, P = 1.00 × 10(-6)), dominant (OR = 2.16, 95% CI = 1.61-2.89, P = 2.22 × 10(-7)), heterozygous (OR = 2.02, 95% CI = 1.55-2.64, P = 2.47 × 10(-7)), and additive genetic models (OR = 1.92, 95% CI = 1.49-2.49, P = 6.70 × 10(-7)). Conclusions: PCSK9 gene E670G polymorphism was associated with an elevated risk of CAD, especially in the Chinese population. More specifically, carriers of the G allele carriers of the PCSK9 gene may be predisposed to developing CAD.

[24] *Bilotta MT, Petillo S, Santoni A, Cippitelli M*. **Liver X Receptors: Regulators of Cholesterol Metabolism, Inflammation, Autoimmunity, and Cancer**. Frontiers in immunology 2020; 11:584303.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33224146

ABSTRACT

The interplay between cellular stress and immune response can be variable and sometimes contradictory. The mechanisms by which stress-activated pathways regulate the inflammatory response to a pathogen, in autoimmunity or during cancer progression remain unclear in many aspects, despite our recent knowledge of the signalling and transcriptional pathways involved in these diseases. In this context, over the last decade many studies demonstrated that cholesterol metabolism is an important checkpoint for immune homeostasis and cancer progression. Indeed, cholesterol is actively metabolized and can regulate, through its mobilization and/or production of active derivatives, many aspects of immunity and inflammation. Moreover, accumulation of cholesterol has been described in cancer cells, indicating metabolic addiction. The nuclear receptors liver-X-receptors (LXRs) are important regulators of intracellular cholesterol and lipids homeostasis. They have also key regulatory roles in immune response, as they can regulate inflammation, innate and adaptive immunity. Moreover, activation of LXRs has been reported to affect the proliferation and survival of different cancer cell types that show altered metabolic pathways and accumulation of

cholesterol. In this minireview we will give an overview of the recent understandings about the mechanisms through which LXRs regulate inflammation, autoimmunity, and cancer, and the therapeutic potential for future treatment of these diseases through modulation of cholesterol metabolism.

[25] *van Hespen KM, Mackaaij C, Waas ISE et al.* **Arterial Remodeling of the Intracranial Arteries in Patients With Hypertension and Controls: A Postmortem Study**. Hypertension 2021; 77:135-146.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33222546
ABSTRACT
The intracranial arteries play a major role in cerebrovascular disease, but arterial remodeling due to hypertension has not been well described in humans. We aimed to quantify this remodeling for: the basilar artery, the vertebral, internal carotid, middle/anterior (inferior)/posterior cerebral, posterior communicating, and superior cerebellar arteries of the circle of Willis. Ex vivo circle of Willis specimens, selected from individuals with (n=24) and without (n=25) a history of hypertension, were imaged at 7T magnetic resonance imaging using a 3-dimensional gradient-echo sequence. Subsequently, histological analysis was performed. We validated the vessel wall thickness and area measurements from magnetic resonance imaging against histology. Next, we investigated potential differences in vessel wall thickness and area between both groups using both techniques. Finally, using histological analysis, we investigated potential differences in arterial wall stiffness and atherosclerotic plaque severity and load. All analyses were unadjusted. Magnetic resonance imaging and histology showed comparable vessel wall thickness (mean difference: 0.04 mm (limits of agreement:-0.12 to 0.19 mm) and area (0.43 mm(2) [-0.97 to 1.8 mm(2)]) measurements. We observed no statistically significant differences in vessel wall thickness and area between both groups using either technique. Histological analysis showed early and advanced atherosclerotic plaques in almost all arteries for both groups. The arterial wall stiffness was significantly higher for the internal carotid artery in the hypertensive group. Concluding, we did not observe vessel wall thickening in the circle of Willis arteries in individuals with a history of hypertension using either technique. Using histological analysis, we observed a difference in vessel wall composition for the internal carotid artery.

[26] *Jamthikar AD, Puvvula A, Gupta D et al.* **Cardiovascular disease and stroke risk assessment in patients with chronic kidney disease using integration of estimated glomerular filtration rate, ultrasonic image phenotypes, and artificial intelligence: a narrative review**. International angiology : a journal of the International Union of Angiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33236868
ABSTRACT
Chronic kidney disease (CKD) and cardiovascular disease (CVD) together result in an enormous burden on global healthcare. The estimated glomerular filtration rate (eGFR) is a well-established biomarker of CKD and is associated with adverse cardiac events. This review highlights the link between eGFR reduction and that of atherosclerosis progression, which increases the risk of adverse cardiovascular events. In general, CVD risk assessments are performed using conventional risk prediction models. However, since these conventional models were developed for a specific cohort with a unique risk profile and further these models do not consider atherosclerotic plaque-based

phenotypes, therefore, such models can either underestimate or overestimate the risk of CVD events. This review examines the approaches used for CVD risk assessments in CKD patients using the concept of integrated risk factors. An integrated risk factor approach is one that combines the effect of conventional risk predictors and noninvasive carotid ultrasound image-based phenotypes. Furthermore, this review provides insights into novel artificial intelligence methods, such as machine learning and deep learning algorithms, to carry out accurate and automated CVD risk assessments and survival analyses in patients with CKD.

[27] *Ling H, Guo Z, Tan L et al.* **Stem cell-derived exosomes: Role in the pathogenesis and treatment of atherosclerosis**. The international journal of biochemistry & cell biology 2020; 130:105884.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33227391
ABSTRACT
Atherosclerosis (AS) is a chronic inflammatory vascular disease characterized by the accumulation of lipids and inflammatory debris in large arteries, high morbidity, and AS-related disease mortality. AS is a complex process, involving endothelial cell dysfunction and inflammation, smooth muscle cell proliferation, and macrophage activation. However, the currently available therapies for AS are not ideal, thus requiring development of novel treatment strategies. Exosomes are bi-lipid membranous extracellular containing multifarious cargo, such as proteins, lipids, micro ribonucleic acid (miRNAs), messenger RNAs, and long non-coding RNAs. Moreover, exosomes reportedly participate in various AS processes. Specifically, stem cell-derived exosomes can regulate the occurrence and development of AS, exhibiting the ability to overcome the limitations associated with AS treatment and stem cell therapy. In this paper, we review the pathological mechanism of AS and discuss the role of exosomes and stem cell-derived exosomes in AS progression. We conclude by suggesting new therapeutic strategies for treating AS with stem cell-derived exosomes in the hope of improving the clinical treatment of AS.

[28] *Langer A, Tan M, Goodman SG et al.* **Does management of lipid lowering differ between specialists and primary care: Insights from GOAL Canada**. Int J Clin Pract 2020:e13861.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33244861
ABSTRACT
BACKGROUND: We studied whether significant differences in care gaps exist between specialists and primary care physicians (PCPs). METHODS: GOAL Canada enrolled patients with CVD or familial hypercholesterolemia (FH) and LDL-C > 2.0 mmol/L despite maximally tolerated statin therapy. During follow-up, physicians received online reminders of treatment recommendations based on Canadian Guidelines. RESULTS: A total of 177 physicians (58% PCPs) enrolled 2009 patients; approximately half of the patients were enrolled by each physician group. Patients enrolled by specialists were slightly older (mean age 63 years vs 62), female (45% vs 40%), Caucasian (77% vs 65%), and had a slightly higher systolic pressure and lower heart rate. Patients enrolled by specialists had less frequent history of FH, diabetes, hypertension, chronic kidney disease and liver disease but more frequent history of coronary artery disease, atrial fibrillation and premature family history of CVD. There was no significant baseline difference in LDL-C, HDL-C or non-HDL-C, although total cholesterol and triglycerides were slightly higher in patients managed by PCPs. At baseline, PCPs were more likely to use statins (80% vs 73%, P = .0002) and other therapies such as niacin or fibrate

(10% vs 6%, P = .0006) but similar use of ezetimibe (24% vs 27%, P = .15). At the end of follow-up, specialists used less statins (70% vs 77%, P = .0005) and other therapies (6% vs 10%, P = .007) but more ezetimibe (45% vs 38%, P = .01) and the same frequency of PCSK9i (28% vs 27%, P = .65). The proportion of patients achieving the recommended LDL-C level of 2.0 mmol/L or below (primary endpoint) was similar at last available visit between specialists and PCPs (44% vs 42%, P = .32). CONCLUSION: Despite minor differences in the clinical profile of their patients, both PCPs and specialists actively participate in the management of lipid-lowering therapy in high-risk CVD patients and experience similar challenges and care gaps.

[29] *Lu Y, Jin X, Zhao P*. **Serum lipids and the pathogenesis of Parkinson's disease: A systematic review and meta-analysis**. Int J Clin Pract 2020:e13865.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33244851
ABSTRACT
BACKGROUND: The role of serum lipids in the pathogenesis of Parkinson's disease (PD) remains unclear, and the results of previous reports remain conflicting. We aimed to conduct this systematic review and meta-analysis to identify the potential relationships of blood lipids and the pathogenesis of PD. METHODS: PubMed, Medline, Web of Science, Cochrane Library, and China National Knowledge Infrastructure (CNKI) databases were searched from inception to March 31, 2020, to identify potential studies with case-control or cohort study design on the relationship of serum lipids and PD. Stata 15.1 software was used for data syntheses after extraction of relevant data. RESULTS: A total of 12 studies with 1506 PD patients and 7330 healthy controls were included. There were no significant differences in the TC (SMD = -0.08, 95% CI [-0.45, 0.33]), LDL-C (SMD = -0.12, 95% CI [-0.46, 0.18]), and TG (SMD = -0.05, 95% CI [-0.18, 0.06]) among PD patients and healthy controls. There was significant difference (SMD = -0.32, 95% CI [-0.42, -0.25]) in the TG level among PD patients and healthy controls. Subgroup analysis by Asian and non-Asian countries indicated that geographical location was not the source of heterogeneity. And no significant publication bias was found (all P > .05). CONCLUSIONS: TG serum levels are significantly lower in PD patients, more studies are needed to further elucidate role of lipid in the PD development.

[30] *Koushki M, Zare M, Shabani M et al.* **Resveratrol Reduces Lipid Accumulation through Upregulating the Expression of MicroRNAs Regulating Fatty Acid Bet Oxidation in Liver Cells: Evidence from In-vivo and In-vitro Studies**. Iranian journal of pharmaceutical research : IJPR 2020; 19:333-340.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33224240
ABSTRACT
MicroRNAs have been shown to regulate lipogenesis in liver. The aim of the present study was to investigate whether the effects of resveratrol (RSV) on lipogenesis are associated with the changes in the expression of two miRNAs (miR-107 and miR-10b) that regulate lipogenic pathways. 30 wild type C57BL/6j male mice were randomly fed three diets: a standard chow diet (ND), a high fat diet (HFD, 60% fat) and the high fat diet supplemented with 0.4% RSV (HFD-RSV) for 16 weeks. HepG2 cells were treated with high glucose (33 mM) and RSV (20 μM) for 24 h. The expression of the genes and miRNAs were measured by real-time PCR. Triglyceride level was increased in the liver of mice and HepG2 cells. In both animal and In-vitro experiments, triglyceride level was significantly decreased in groups treated with RSV. The expression of the miR-107 and miR-10b was significantly upregulated

in the liver of HFD mice, whereas HFD-RSV group demonstrated a significant lower expression of both miRNAs compared to HFD group. In addition, RSV treatment significantly upregulated the expression of CPT-1a and PPARα genes in the liver of HFD mice. Moreover, treatment with RSV could reduce the expression of miR-107 and miR-10b and increase the expression of CPT-1a and PPARα in HG-treated HepG2 cells. These evidence, as a whole, suggest that RSV could exert its anti-lipogenic effect partially through alterations in the expression of miR-107 and miR-10b in liver cells.

[31] *Huded CP, Shah NP, Puri R et al.* **Association of Serum Lipoprotein (a) Levels and Coronary Atheroma Volume by Intravascular Ultrasound**. Journal of the American Heart Association 2020; 9:e018023.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33222598
ABSTRACT
Background Lp(a) (lipoprotein (a)) is a risk factor for cardiovascular events, but the mechanism of increased risk is uncertain. This study evaluated the relationship between Lp(a) and coronary atheroma volume by intravascular ultrasound. Methods and Results This was a post hoc analysis of 6 randomized trials of coronary atheroma by intravascular ultrasound. The population was stratified into high (≥60 mg/dL) and low (<60 mg/dL) baseline serum Lp(a). The primary outcome was baseline coronary percent atheroma volume. A mixed model adjusted for baseline low density lipoprotein, ApoB (apoliporotein B100), non-high density lipoprotein, sex, age, race, history of myocardial infarction, statin use, and intravascular ultrasound study was used to provide estimates of baseline plaque burden. Of 3943 patients, 17.3% (683) had Lp(a) ≥ 60 mg/dL and 82.7% (3260) had Lp(a) < 60 mg/dL. At baseline, uncorrected low density lipoprotein level (107.7 ± 32.0 versus 99.1 ± 31.5) and statin therapy (99.0% versus 97.0%) were higher in patients with high Lp(a) levels, but low density lipoprotein corrected for Lp(a) was lower (80.6 ± 32.0 versus 94.0 ± 31.4) in patients with high Lp(a) levels. Percent atheroma volume was significantly higher in the high Lp(a) group in unadjusted (38.2% [32.8, 43.6] versus 37.1% [31.4, 43.1], P=0.01) and risk-adjusted analyses (38.7%±0.5 versus 37.5%±0.5, P<0.001). There was a significant association of increasing risk-adjusted percent atheroma volume across quintiles of Lp(a) (Lp(a) quintiles 1-5; 37.3 ± 0.5%, 37.2 ± 0.5%, 37.3 ± 0.5%, 38.0 ± 0.5%, 38.5 ± 0.5%, P=0.002). Conclusions Elevated Lp(a) is independently associated with increased percent atheroma volume. Further work is needed to clarify the relationship of Lp(a)-lowering treatment with cardiovascular outcomes.

[32] *Danyer E, Bilal T*. **Effects of dietary fish oil and alpha-tocopherol supplementation on selected blood parameters and fatty acid profiles in mares and their foals**. J Anim Physiol Anim Nutr (Berl) 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33225499
ABSTRACT
The effects of fish oil (40 ml/day) supplementation, with or without synthetic all-rac-alpha-tocopherol-acetate (2,500 IU/day), during the last 65 days before expected parturition were investigated in 15 adult mares (553 ± 24 kg BW) and their foals. Mares were assigned to one of three diets: control (n = 5), control plus fish oil and alpha-tocopherol (n = 4; FO + AT) or control with just fish oil (n = 6; FO). Blood samples were obtained from the mares before a 15-day dietary adaptation period (T1) and from mares and foals the first (T2) and fifth (T3) days post-partum. Colostrum was collected at T2

and milk at T3. Routine haematological, biochemical and alpha-tocopherol analyses were undertaken on all blood samples. Fatty acid concentrations were determined in the foal serum and alpha-tocopherol concentrations measured in the milk and colostrum. Diet had no effect on haematology or biochemistry in the mares. Alpha-tocopherol concentrations were significantly higher at T2 & T3 in the FO + AT mares. Foal WBCs were higher in FO (11.33 ± 2.59 × 10(9) /l), comparing to FO + AT and control groups (9.18 ± 1.24 × 10(9) /l and 7.26 ± 1.03 × 10(9) /l, respectively), at T3 ($p < .05$). There was no significant effect of the fish oil supplementation on the foal's serum fatty acid profile. In the FO + AT group, both colostrum and milk alpha-tocopherol concentrations (2.56 ± 0.36 and 1.36 ± 0.22 μg/ml, respectively) were higher compared than those of the FO group (1.33 ± 0.39 and 0.72 ± 0.31 μg/ml, respectively; $p < .05$). Additional 2,500 IU/day of synthetic alpha-tocopherol in the last 65 days of pregnancy increased alpha-tocopherol concentrations in colostrum and milk and the foal's serum. 40 ml/day fish oil, however, did not significantly increase serum eicosapentaenoic acid and docosahexaenoic acid concentrations in the foals.

[33] *Hirata KI*. **New Evidence of Probucol on Cardiovascular Events**. Journal of atherosclerosis and thrombosis 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33229816
ABSTRACT

[34] *Jiménez-Vacas JM, Herrero-Aguayo V, Montero-Hidalgo AJ et al.* **Clinical, cellular and molecular evidence of the additive antitumor effects of biguanides and statins in prostate cancer**. The Journal of clinical endocrinology and metabolism 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33247590
ABSTRACT
CONTEXT: Prostate cancer (PCa) is one of the leading causes of cancer-related death among male population worldwide. Unfortunately, current medical treatments fail to prevent PCa progression in a high percentage of cases; therefore, new therapeutic tools to tackle PCa are urgently needed. Biguanides and statins have emerged as antitumor agents for several endocrine-related cancers. OBJECTIVE: To evaluate: i) the putative in vivo association between metformin and/or statins treatment and key tumor and clinical parameters, and ii) the direct effects of different biguanides (metformin/buformin/phenformin), statins (atorvastatin/simvastatin/lovastatin), and their combination, on key functional endpoints and associated signalling mechanisms. METHODS: An exploratory/observational retrospective cohort of patients with PCa (n=75) was analysed. Moreover, normal and tumor prostate cells [normal (RWPE-cells/primary prostate cell-cultures); tumor (LNCaP/22RV1/PC3/DU145 cell-lines)] were used to measure proliferation/migration/tumorsphere-formation/signalling pathways. RESULTS: The combination of metformin+statins in vivo was associated to lower Gleason-score and longer biochemical recurrence-free survival. Moreover, biguanides and statins exerted strong antitumor actions (i.e. inhibition of proliferation/migration/tumorspheres-formation) on PCa cells, and that their combination further decreased, additively, these functional parameters compared with the individual treatments. These actions were mediated through modulation of key oncogenic and metabolic signalling-pathways (i.e. AR/mTOR/AMPK/AKT/ERK) and molecular mediators (MKI67/cMYC/androgen-receptor/cell-cycle inhibitors). CONCLUSIONS: Biguanides and statins significantly reduced tumor aggressiveness in PCa, being this effect more potent (in vitro and in vivo) when both compounds are combined.

Therefore, given the demonstrated clinical safety of biguanides and statins, our results suggest a potential therapeutic role of these compounds, especially their combination, for the treatment of PCa.

[35] *Zafrir B, Egbaria A, Stein N et al.* **PCSK9 inhibition in clinical practice: Treatment patterns and attainment of lipid goals in a large health maintenance organization**. Journal of clinical lipidology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33243717
ABSTRACT
BACKGROUND: Proprotein convertase subtilisin/kexin type-9 inhibitors (PCSK9i) effectively reduce low-density lipoprotein cholesterol (LDL-C), improving cardiovascular outcomes in clinical trials when added to statin therapy. OBJECTIVES: As real-world evidence is lacking, we aimed to evaluate treatment and adherence patterns using PCSK9i in clinical practice. METHODS: We investigated 1600 patients initiating PCSK9i between January 2016 and December 2019 in a large health maintenance organization. Treatment discontinuation was defined as a gap ≥60 days between last days' supply of one prescription and the start of the next. Re-initiation rates as well as proportion of days covered (PDC) over 1-year period and attainment of lipid goals under PCSK9i, were analyzed. RESULTS: Evolocumab 140 mg was initiated by 50.7%, alirocumab 75 mg by 29.5% and 150 mg by 19.8%. Cumulative discontinuation rates were 28.1% after 6-months and 49.9% after 3-years. Overall, 58% of the patients that discontinued therapy have re-initiated PCSK9i (31% after 3-months from discontinuation). Mean PDC over 1-year of therapy was 56% ± 29, with PDC ≥80% evident in 29%. Of those with established cardiovascular disease (n = 991), 55% achieved LDL-C<70 mg/dL and 38% LDL-C<55 mg/dL. Attainment rates were lower in patients with PDC<80%, baseline LDL-C>190 mg/dL and in those not treated with concurrent statin therapy. CONCLUSIONS: In real-world practice of patients treated by PCSK9i, high proportion of early treatment discontinuation was evident, with non-negligible re-initiation rates but overall low medication coverage over time. This have contributed to sub-optimal attainment of LDL-C treatment goals, particularly observed in patients with severe hypercholesterolemia, inadequate drug adherence, and those using PCSK9i as monotherapy.

[36] *Onishi S, Tajika M, Bando H et al.* **Ursodeoxycholic acid and bezafibrate were useful for steroid-refractory, immune-related hepatitis: a case report**. Journal of medical case reports 2020; 14:230.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33239098
ABSTRACT
BACKGROUND: Immune checkpoint inhibitors have shown clinically significant antitumor efficacy and have been approved for the treatment of various kinds of advanced malignancies. On the other hand, these immunotherapies show unique adverse events, termed "immune-related adverse events," which are distinctly associated with conventional cytotoxic chemotherapy. Hepatotoxicity is recognized as an immune-related adverse event; prompt treatment with corticosteroids is recommended. However, some cases are refractory to steroids. Here, we report the first case (to our knowledge) of steroid-refractory immune-related hepatitis that was successfully treated with ursodeoxycholic acid and bezafibrate. CASE PRESENTATION: A 68-year-old Asian man, came to our hospital for the treatment of malignant melanoma involving the gingiva and presenting with multiple lymph node and bone metastases was administered nivolumab as a first-line treatment. Two months into treatment, the patient developed diarrhea as a result of immune-related colitis; the colitis

was treated successfully with prednisolone 60 mg/ day, resulting in improvement in the patient's symptoms. However, when steroids were being tapered, acute elevation of liver enzymes was observed. Autoimmune hepatitis was suspected as an immune-related adverse event, and treatment with intravenous prednisolone 60 mg/ day was reinitiated. However, restoration of the steroid treatment failed to improve the patient's liver enzymes. On the basis of histological findings from liver biopsy and exclusion of other etiologies such as viral infection and other drug-induced hepatitis, steroid-refractory hepatic immune-related adverse event was deemed the most likely cause of the patient's acute hepatitis. In general, mycophenolate mofetil or tacrolimus is known to provide benefits in cases of steroid-refractory hepatitis. We therefore decided to add oral ursodeoxycholic acid and bezafibrate in consideration of the patient's background of repeated aspiration pneumonia. Administration of this regimen resulted in an improvement in liver function, which remained normal even after tapering of prednisolone. CONCLUSIONS: Ursodeoxycholic acid and bezafibrate may be useful for treatment of steroid-refractory immune-related adverse event hepatitis.

[37] *Azmi S, Ferdousi M, Kalteniece A et al.* **Protection from neuropathy in extreme duration type 1 diabetes**. J Peripher Nerv Syst 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33236478
ABSTRACT
A proportion of individuals with type 1 diabetes mellitus for more than 50 years (medallists) may be protected from developing nephropathy, retinopathy and neuropathy. Detailed neuropathy phenotyping was undertaken in a cohort of 33 medallists aged 63.7 ± 1.4 years with diabetes for 58.5 ± 0.8 years and HbA1c of 65.9 ± 2.1 mmol/mmol. Medallists had a significantly higher HbA1c ($P < .001$), lower estimated glomerular filtration rate (eGFR) ($P = .005$) and higher albumin creatinine excretion ratio (ACR) ($P = .01$), but a lower total cholesterol ($P < .001$), triacylglycerols ($P = .001$), low density lipoprotein-cholesterol ($P < .001$) and higher high density lipoprotein-cholesterol ($P = .03$), compared to controls. Twenty-four percent of participants were identified as "escapers" without confirmed diabetic neuropathy. They had a lower neuropathy symptom profile ($P = .002$), vibration perception threshold ($P = .02$), warm threshold ($P = .05$), higher peroneal amplitude ($P = .005$), nerve conduction velocity ($P = .03$), heart rate variability ($P = .001$), corneal nerve fibre density ($P = 0.001$), branch density ($P < .001$) and length ($P = .001$), compared to medallists with diabetic neuropathy. Escapers had a shorter duration of diabetes ($P = .006$), lower alcohol consumption ($P = .04$), lower total cholesterol ($P = .04$) and LDL ($P = .02$), higher eGFR ($P = .001$) and lower ACR ($P < .001$). Patients with extreme duration diabetes without diabetic neuropathy have a comparable HbA1c, blood pressure and body mass index, but a more favourable lipid profile and consume less alcohol compared to those with diabetic neuropathy.

[38] *Afshinnia F, Jadoon A, Rajendiran TM et al.* **Plasma lipidomic profiling identifies a novel complex lipid signature associated with ischemic stroke in chronic kidney disease**. J Transl Sci 2020; 6.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33240530
ABSTRACT
RATIONALE AND OBJECTIVE: Despite contribution of dyslipidemia to ischemic stroke, plasma lipidomic correlates of stroke in CKD is not studied. This study is aimed to identify plasma lipid alterations associated with stroke. STUDY DESIGN: Cross sectional. SETTING AND POPULATION:

214 participants of Clinical Phenotyping and Resource Biobank Core (CPROBE). Clinical data and plasma samples at the time of recruitment were obtained and used to generate lipidomic data by liquid chromatography/mass-spectrometry-based untargeted platform. PREDICTORS: Various levels of free fatty acids, acylcarnitines and complex lipids. OUTCOME: Stroke. ANALYTIC APPROACH: includes compound by compound comparison of lipids using t-test adjusted by false discovery rate in patients with and without stroke, and application of logistic regression analysis to identify independent lipid predictors of stroke and to estimate the odds associated with their various levels. RESULTS: Overall, we identified 330 compounds. Enrichment analysis revealed overrepresentation of differentially regulated phosphatidylcholines (PC)s and phosphatidylethanolamines (PE)s were overrepresented in stroke (P<0.001). Abundance of PC38:4, PE36:4, PC34:0, and palmitate were significantly higher, but those of plasmenyl-PE (pPE)38:2, and PE 32:2 was significantly lower in patients with stroke (p≤0.0014). After adjusting, each 1-SD increase in palmitate and PC38:4 was independently associated with 1.84 fold (95% CI: 1.06-3.20, p=0.031) and 1.84 fold (1.11-3.05, p=0.018) higher risk of stroke, respectively. We observed a significant trend toward higher abundance of PCs, PEs, pPEs, and sphingomyelins in stroke (p≤0.046). LIMITATIONS: Small sample size; unclear, if similar changes in the same or opposite direction preceded stroke, as the cross-sectional nature of the observation does not allow determining the effect of time course on lipid alterations. CONCLUSION: Differential regulation of palmitate, PCs, and PEs in patients with CKD and a history of stroke may represent a previously unrecognized risk factor and might be a target of risk stratification and modification.

[39] *O'Connor EA, Evans CV, Rushkin MC et al.* **Behavioral Counseling to Promote a Healthy Diet and Physical Activity for Cardiovascular Disease Prevention in Adults With Cardiovascular Risk Factors: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force**. Jama 2020; 324:2076-2094.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33231669

ABSTRACT

IMPORTANCE: Cardiovascular disease is the leading cause of death in the US, and poor diet and lack of physical activity are major factors contributing to cardiovascular morbidity and mortality. OBJECTIVE: To review the benefits and harms of behavioral counseling interventions to improve diet and physical activity in adults with cardiovascular risk factors. DATA SOURCES: MEDLINE, PubMed, PsycINFO, and the Cochrane Central Register of Controlled Trials through September 2019; literature surveillance through July 24, 2020. STUDY SELECTION: English-language randomized clinical trials (RCTs) of behavioral counseling interventions to help people with elevated blood pressure or lipid levels improve their diet and increase physical activity. DATA EXTRACTION AND SYNTHESIS: Data were extracted from studies by one reviewer and checked by a second. Random-effects meta-analysis and qualitative synthesis were used. MAIN OUTCOMES AND MEASURES: Cardiovascular events, mortality, subjective well-being, cardiovascular risk factors, diet and physical activity measures (eg, minutes of physical activity, meeting physical activity recommendations), and harms. Interventions were categorized according to estimated contact time as low (≤30 minutes), medium (31-360 minutes), and high (>360 minutes). RESULTS: Ninety-four RCTs were included (N = 52 174). Behavioral counseling interventions involved a median of 6 contact hours and 12 sessions over the course of 12 months and varied in format and dietary recommendations; only 5% addressed physical activity alone. Interventions were associated with a lower risk of cardiovascular

events (pooled relative risk, 0.80 [95% CI, 0.73-0.87]; 9 RCTs [n = 12 551]; I2 = 0%). Event rates were variable; in the largest trial (Prevención con Dieta Mediterránea [PREDIMED]), 3.6% in the intervention groups experienced a cardiovascular event, compared with 4.4% in the control group. Behavioral counseling interventions were associated with small, statistically significant reductions in continuous measures of blood pressure, low-density lipoprotein cholesterol levels, fasting glucose levels, and adiposity at 12 to 24 months' follow-up. Measurement of diet and physical activity was heterogeneous, and evidence suggested small improvements in diet consistent with the intervention recommendation targets but mixed findings and a more limited evidence base for physical activity. Adverse events were rare, with generally no group differences in serious adverse events, any adverse events, hospitalizations, musculoskeletal injuries, or withdrawals due to adverse events. CONCLUSIONS AND RELEVANCE: Medium- and high-contact multisession behavioral counseling interventions to improve diet and increase physical activity for people with elevated blood pressure and lipid levels were effective in reducing cardiovascular events, blood pressure, low-density lipoproteins, and adiposity-related outcomes, with little to no risk of serious harm.

[40] *Kochergin NA, Kochergina AM, Ganyukov VI, Barbarash OL*. **[Predictors of Coronary Plaque Vulnerability in Patients with Stable Coronary Artery Disease]**. Kardiologiia 2020; 60:20-26.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33228501
ABSTRACT
Aim To identify new predictors for vulnerability of atherosclerotic coronary plaques in patients with stable ischemic heart disease (sIHD).Material and methods This prospective, single-center study included 58 patients with sIHD. Unstable plaques were detected with virtual histology intravascular ultrasound of proximal and medium segments of a coronary artery without significant lesions according to coronarography data. Indexes of inflammation, dyslipidemia and carbohydrate metabolism were considered as candidate predictors for coronary plaque vulnerability.Results In 56 coronary arteries, 58 plaques were detected, 12 of which (20.7%) were unstable. Vulnerable plaques differed morphologically from stable ones by a greater size of the necrotic core (35.1±8.5% vs. 24.0±13.2%; p=0.008), calcified nodules (2.0 [1.0; 5.0] % vs. 1.0 [0; 2.0] %; p=0.006), and a lower content of fibrous components (54.9±10.2% vs. 66.4±15.8%; p=0.02). In addition, vulnerable plaques more frequently narrowed the arterial lumen by >70% of the lumen area (33.3% vs. 2.2%; p=0.0006). Correlation analysis showed a negative correlation between the level of high-density lipoproteins (HDL) and calcium volume (r= -0.4104; p=0.023); a positive correlation between the blood glucose level as determined by the oral glucose tolerance test and the lipid component (r=0.48198; p=0.033); and a negative correlation between the apolipoprotein A level and the calcium volume (r= -0.4297; p=0.008).Conclusion The study demonstrated a high prevalence of vulnerable plaques in nontarget coronary arteries in patients with sIHD. In this process, dyslipidemia indexes (LDL, apolipoproteins A) correlate with the calcium volume whereas blood glucose, as measured in the oral glucose tolerance test, correlates with the lipid component of coronary plaque.

[41] *Mareev VY, Mareev YV*. **[Influence of Omega-3 PUFA on Non-invasive factors determining the risk of arrhYthmias eXcess and sudden cardiac death in patients with HFpEF with ischemic etiology (ONYX)]**. Kardiologiia 2020; 60:86-98.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33228511
ABSTRACT

Aim Patients with heart failure with reduced left ventricular (LV) ejection fraction (HFrEF) who have had acute myocardial infarction have an unfavorable prognosis, largely due to ventricular arrhythmias (VA) and risk of sudden cardiac death (SCD). The optimal treatment (triple neurohormonal blockade plus implantable cardioverter defibrillator and cardiac resynchronization therapy) reduced the risk of SCD primarily due to reverse cardiac remodeling, but has not solved this problem completely. Efficacy of purified ω-3 polyunsaturated fatty acid esters (PUFA) in low doses (1 g/day) in reducing VA and risk of SCD in HFrEF patients was demonstrated in two large randomized clinical trials. The PUFA effects was suggested to be related also with increased heart rhythm variability (HRV) and chronotropic action, which might depend on the drug dose. The present open, prospective, randomized, comparative study in parallel groups evaluated the effect of Omacor in different doses on noninvasive markers of SCD risk in patients with ischemic HFrEF receiving the optimal drug therapy.Methods Patients (n=40) were randomized at a 1:1:2 ratio to the control group (n=10), the Omacor 1 g/day treatment group (n=10), and the Omacor 2 g/day treatment group (n=20) and were followed up for 12 months. Clinical evaluation included changes in the CHF functional class (FC) and Clinical Condition Scale (CCS) score; concentration of N-terminal pro-hormone brain natriuretic peptide (NT-proBNP); and peak oxygen consumption during exercise (peak VO2). The LV function was evaluated by LVEF. Holter ECG monitoring was used for evaluation of HRV (SDNN), average 24-h heart rate (HR), number of ventricular extrasystoles (VE) per hour and severity of VA, and presence of paired VE and VT runs.Results Improvement of CHF FC became significant only with the high-dose Omacor treatment (2 g/day). The CCS score showed a tendency towards decrease also with a lower dose (1 g/day) whereas the level of NT-proBNP significantly decreased with both Omacor doses. The increase in LV EF was significant only with the use of Omacor 2 g/day (+3%, p=0.002). A negative chronotropic effect of ω-3 PUFA was observed. Average 24-h HR decreased by 8 bpm (p=0.05) and 11 bpm (p<0.001) with Omacor 1 g/day and 2 g/day, respectively. Either dose of ω-3 PUFA significantly improved VO2, which directly correlated with LV EF and inversely correlated with HR. The decrease in number of VE was associated not only with improved HRV (SDNN) but also with the decrease in 24-h HR, and thus Omacor 2 g/day significantly decreased the number of VE (by 16 per hour) and dangerous VA (paired VE and VT runs ceased to be detected in 40% of patients).Conclusion Since HR, HRV, and VA are closely interrelated, the effect of ω-3 PUFA specifically on these noninvasive markers apparently determines its ability to decrease the risk of SCD in patients with ischemic HFrEF. The antiarrhythmic effect of Omacor was greater with higher doses of this drug.

[42] *Kopylov VY*. **Changes in the functional state of the epithelium of the proximal renal tubules in patients with the initial stage of chronic heart failure during simvastatin therapy**.
Klinicheskaia laboratornaia diagnostika 2020; 65:602-606.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33245648

ABSTRACT

To assess the change in the functional state of the proximal renal tubule epithelium in patients with dyslipidemia on the background of obesity, by determining the concentration in the urine of the examined level of cystatin C and the degree of activity of the renal organ-specific enzymes neutral α-glucosidase (NAG) and L-alaninaminopeptidase (laap) during simvastatin therapy at a daily dose of 20 mg for 6 months. The study involved 88 people who were divided into three groups: control, comparison and main. The control group is a group of practically healthy individuals: 30 people,

average age 20.67 ± 0.18 years, body mass index (BMI) 21.36 ± 0.4 kg/m2. Comparison group (obese): 27 people, average age 22.38 ± 0.76 years, BMI 31.48 ± 0.56 kg / m2. Patients of the main group were divided into 2 subgroups. The first main subgroup of persons with chronic heart failure stage I (CHF I) without type 2 diabetes mellitus (DM 2)) - 15 observed: average age 56.8 ± 1.8 years, BMI 30.28 ± 1.11 kg / m2. The second main subgroup (CHF I with DM 2) - 16 observed: average age 48.25 ± 2.45 years, BMI 30.37 ± 1.11 kg/m2. The study found that simvastatin therapy does not affect glomerular filtration rate in patients with asymptomatic heart dysfunction. There was an increased level of cystatin C in the urine of the comparison group compared to the control group, the concentration of cystatin C in the main subgroups was statistically significantly higher than the control group. On the background of simvastatin therapy for 6 months, the level of this analyte is statistically significantly increased. The activity of LAAP and NAG during simvastatin therapy during the follow-up period in the CHF I subgroup without DM2 significantly decreased. In the subgroup of CHF I + DM2, a decrease in the concentration of LAAP and an increase in the activity of NAG was revealed, which may indicate that the brush border epithelium dystrophy occurred during simvastatin therapy. Simvastatin therapy for 6 months in patients with the initial stage of heart failure at a daily dosage of 20 mg does not impair glomerular function in the form of reduced glomerular filtration rate (GFR). Cystatin C levels are higher in obese individuals without heart failure and significantly higher in those with asymptomatic heart failure. When treating dyslipidemia with simvastatin at a dose of 20 mg / day, there is a decrease in the activity of NAG and laap in patients with CHF I without DM2. In the result of lipid-lowering therapy with simvastatin in a daily dosage of 20 mg in patients with CHF I+D2M there is increased activity of NAG while reducing the concentration of the LAAP, which may be due to degeneration of the proximal tubular epithelium, amid additional load on a partially renal route of metabolism of simvastatin.

[43] *Ahn SH, Lee JH, Lee JW*. **Inverse association between triglyceride glucose index and muscle mass in Korean adults: 2008-2011 KNHANES**. Lipids in health and disease 2020; 19:243. **PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33222694

ABSTRACT

BACKGROUND: Since sarcopenia is an important risk factor for falls or cardiovascular disease, early detection and prevention of sarcopenia are being increasingly emphasized. Emerging evidence has indicated relationships between sarcopenia, insulin resistance, and inflammation. The triglyceride glucose (TyG) index, a novel surrogate marker of insulin resistance and systemic inflammation, has not yet been shown to be associated with sarcopenia. This study aimed to examine the relationship between the TyG index and muscle mass in Korean adults. METHODS: This study included 15,741 non-diabetic adults over 19 years old using data from the 2008-2011 Korea National Health and Nutrition Examination Survey. Participants were divided into three groups according to tertiles of the TyG index. A low skeletal muscle mass index (LSMI) was defined by the Foundation for the National Institutes of Health Sarcopenia Project criteria. A weighted multivariate logistic regression model was used to analyze relationships between TyG index tertiles and LSMI. RESULTS: The ORs (95% CIs) for LSMI in the second and third TyG tertiles, compared to the first tertile, were 1.463 (1.131-1.892) and 1.816 (1.394-2.366), respectively, after adjusting for confounding factors. Higher TyG index values were also associated with increased odds of LSMI in adults under 65 years who did not exercise regularly, who consumed less than 30 g of alcohol per day, who did not currently smoke, and

who ate less than 1.5 g of protein/kg/day. CONCLUSION: The TyG index was significantly and positively associated with LSMI in Korean adults.

[44] *Deng Y, Liu W, Wang J et al.* **Intermittent Fasting Improves Lipid Metabolism Through Changes in Gut Microbiota in Diet-Induced Obese Mice**. Medical science monitor : international medical journal of experimental and clinical research 2020; 26:e926789.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33223514
ABSTRACT
BACKGROUND The mechanism of how intermittent fasting (IF) improves metabolism is not fully understood. Our study aimed to explore the effect of IF on lipid metabolism in obese mice, specifically on the intestinal flora. MATERIAL AND METHODS Diet-induced obese (DIO) mice were subjected to ad libitum (AL) feeding or IF (alternate-day fasting) for 30 days. We examined the lipid metabolism, fat distribution, gene expression of lipid metabolism, and intestinal flora in the mice. RESULTS Despite having access to the same high-fat diet as the AL-fed groups, IF mice displayed pronounced weight loss, and their lipid metabolism significantly improved, mainly reflected in lower serum lipid levels and ameliorated liver steatosis. IF also reduced metabolic endotoxemia in DIO mice. The 16S ribosomal deoxyribonucleic acid gene amplicon sequencing suggested that IF did not change the community richness but had a tendency to increase community diversity in the intestinal flora. In addition, IF significantly reduced the ratio of Firmicutes to Bacteroidetes and increased the relative abundance of Allobaculum in the intestinal flora. CONCLUSIONS IF can improve fat metabolism, reduce fat accumulation, promote white fat conversion to beige, and improve gut microbiota.

[45] *Ciucanu CI, Olariu S, Vlad DC, Dumitraşcu V*. **Influence of rosuvastatin dose on total fatty acids and free fatty acids in plasma: Correlations with lipids involved in cholesterol homeostasis**. Medicine (Baltimore) 2020; 99:e23356.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33235104
ABSTRACT
This study investigates for the first time the influence of four doses of rosuvastatin on total fatty acids (TFA) and free fatty acids (FFA) in human plasma and correlates their changes in concentration with changes in the concentration of other lipids involved in cholesterol homeostasis.This study was a placebo-controlled, randomized, double-blind, crossover experiment. The study used a single group of 16 men and consisted of 5 treatment periods lasting 4 weeks each with placebo and 4 doses of rosuvastatin (5, 10, 20, and 40 mg). Each subject changed 5 medical treatments and received in each new treatment different tablets of rosuvastatin or placebo compared to those taken in previous treatments, in a random order. Between treatment periods there was a wash-out period of 2 weeks, without treatment.Changes in TFA and FFA were significant compared to placebo and between different doses of rosuvastatin. We found a continuous logarithmic decrease in levels of TFA, FFA, low-density lipoprotein (LDL)-cholesterol, total cholesterol, triglycerides, phospholipids, and apolipoprotein B-100, and a continuous increase in levels of high-density lipoprotein (HDL)-cholesterol and apolipoprotein A-1 by increases the dose of rosuvastatin. Analysis of the correlation of TFA and FFA with the main lipids and lipoproteins in cholesterol homeostasis indicated a linear regression with high correlation coefficients and all P-values were less than .05 level.The concentrations of TFA and FFA are significantly influenced by the dose of rosuvastatin. They are strongly correlated with those of other lipids and lipoproteins involved in cholesterol homeostasis. The

mechanisms of cholesterol homeostasis regulation are involved in changing the concentrations of TFA and FFA.

[46] *Arellano J, Carrasco C, García C*. **[A report of successful management with simvastatin plus ezetimibe in alopecia areata]**. Medwave 2020; 20:e8053.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33231574
ABSTRACT
Alopecia areata is a common type of non-scarring alo¬pecia. Although the exact pathogenesis remains elusive, alopecia areata is thought to have a multifactorial etiology described as an interplay of genetic predisposition and environmental exposures. In patients with genetic susceptibility, stress, infection, and microtrauma have been documented to decrease immunosuppressive cytokines that generally maintain the hair follicle's immune privilege. There is currently no curative therapy for alopecia areata, although some treatments can induce hair growth in a percentage of patients. It has been postulated that simvastatin reestablishes the immune privilege, and ezetimibe would provide an immunomodulatory and anti-inflammatory effect. We report a case of a 23 years-old woman with alopecia areata successfully treated with simvastatin/ezetimibe.

[47] *de Paiva Silvino JP, Jannes CE, Tada MT et al.* **Cascade screening and genetic diagnosis of familial hypercholesterolemia in clusters of the Southeastern region from Brazil**. Molecular biology reports 2020; 47:9279-9288.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33231818
ABSTRACT
Familial hypercholesterolemia (FH) is an autosomal dominant genetic disease characterized by high levels of low-density lipoprotein-cholesterol (LDLc), associated to premature cardiovascular disease. The detection of the variants related to FH is important to improve the early diagnosis in probands / index-cases (ICs) and their relatives. We included ICs with FH and their relatives, living in a small region of Minas Gerais state-Brazil, which were classified according to Dutch Lipid Clinic Network Criteria (DLCNC) and submitted to sequencing of genes related to FH (LDLR, APOB, PCSK9, LDLRAP1, LIPA, STAP1, APOE, ABCG5 e ABCG8). In a total of 143 subjects (32 ICs and 111 relatives), eight variants were identified in 91 individuals. From these variants, five were in LDLR [p.(Asp224Asn), p.(Ser854Gly), p.(Cys34Arg), p.(Asp601His), deletion of exon15 in LDLR)], one in APOB [p.(Met499Val)], one in PCSK9 [p.(Arg237Trp)] and one in APOE [p.(Pro28Leu)] genes. The variants were detected in 100% of those subjects classified as definitive, 87% as probable and 69% as possible FH cases based on DLCNC. The LDLc level was higher in individuals with corneal arch and xanthomas or xanthelasmas, as well as in pathogenic or probably pathogenic variants carriers. This study showed higher frequency of LDLR gene variants compared to other genes related to LDL metabolism in individuals with FH in Minas Gerais - Brazil and the presence of FH in relatives without previous diagnosis. Our data reinforce the importance of molecular and clinical evaluation of FH relatives in order to early diagnosis the FH, as well as cardiovascular diseases prevention.

[48] *Lim GB*. **Lipid lowering remains effective in older patients**. Nature reviews. Cardiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33235373
ABSTRACT

[49] *Craveiro V, Ramos E, Araújo J.* **Metabolically healthy overweight in young adulthood: is it a matter of duration and degree of overweight?** Nutrition, metabolism, and cardiovascular diseases : NMCD 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33229201
ABSTRACT
BACKGROUND AND AIM: Given the controversy regarding metabolically healthy obesity, we studied the association between duration and degree of body mass index (BMI) from adolescence to early adulthood and metabolic status of both overweight/obese and under/normal weight subjects. METHODS AND RESULTS: Participants of the EPITeen cohort were evaluated at 13, 17, 21 and 24 years (n = 1040). Duration and degree of BMI in the 11-year period was summarized through the area under the curve of BMI (BMI(AUC)). Metabolic health at 24 y was defined as optimal levels of lipids, blood pressure and glucose. The association between BMI(AUC) per year and metabolic health was estimated through binary logistic regression models, adjusted for confounders and stratified by BMI. The proportion of metabolically healthy overweight/obesity at 24 y was 13.4%. After adjustment for sociodemographic and behavioural factors, the increase of one kg/m(2) in BMI on average per year during the period between 13 and 24 y was associated with 14% lower odds of being metabolically healthy among under/normal weight participants (OR = 0.86, 95% CI 0.78-0.94); and 8% lower odds of metabolic health among obese/overweight participants (OR = 0.92, 95% CI 0.85-1.00). After additional adjustment for waist circumference, the association was attenuated, especially in the obese/overweight group (OR = 1.03, 95% CI 0.93-1.14). About 20% of the metabolically healthy obese/overweight at 13 y transitioned to metabolically unhealthy obesity/overweight at 24 y. CONCLUSION: The results support the hypothesis that the healthy obesity phenotype could be explained by a lower exposure to adiposity, either by shorter time or lower quantity, and a more favourable body fat distribution.

[50] *Du Y, Lv Y, Zha W et al.* **Effect of coffee consumption on dyslipidemia: A meta-analysis of randomized controlled trials**. Nutrition, metabolism, and cardiovascular diseases : NMCD 2020; 30:2159-2170.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33239163
ABSTRACT
BACKGROUND AND AIM: Dyslipidemia is a common metabolic disease worldwide and also an important predisposing factor for cardiovascular diseases (CVDs). Coffee is loved by people all over the world; however, the association between coffee consumption and blood lipids has yielded inconsistent results. So we carried this meta-analysis to explore the effects of coffee consumption on blood lipids. METHODS AND RESULTS: Medline, PubMed, Web of science, Embase, and Cochrane Library databases were systematically searched until April 2020. Combined weighted mean differences (WMD) with their 95% confidence interval (CI) were calculated using random-effects models, and between-study heterogeneity was assessed by Cochran's Q test and I(2) statistics. Subgroup analysis and meta-regression analysis were also conducted to explore the potential heterogeneity. A total of 12 RCT studies involving the association between coffee consumption and blood lipid levels were included in the meta-analysis. The pooled results showed that coffee consumption significantly increased total cholesterol (TC) (WMD: 0.21 mmol/L, 95% CI: 0.04; 0.39, P = 0.017), triglyceride (TG) (WMD: 0.12 mmol/L, 95% CI: 0.03; 0.20, P = 0.006) and low-density lipoprotein (LDL-C) (WMD: 0.14 mmol/L, 95% CI: 0.05; 0.24, P = 0.003) while had no significant effect

on high-density lipoprotein (HDL-C) (WMD: -0.01 mmol/L, 95% CI: -0.06; 0.04, P = 0.707). Dose-response analysis results revealed significant positive nonlinear associations between coffee consumption and the increase in TC, LDL-C, and TG levels. CONCLUSIONS: Evidence from this meta-analysis suggested that coffee consumption may be associated with an elevated risk for dyslipidemia and CVDs. So a reasonable habit of coffee consumption (<3 cups/d) is essential for the prevention of dyslipidemia.

[51] *Møller G, Ritz C, Kjølbæk L et al.* **Sagittal abdominal diameter and waist circumference appear to be equally good as identifiers of cardiometabolic risk**. Nutrition, metabolism, and cardiovascular diseases : NMCD 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33223400
ABSTRACT
BACKGROUND AND AIMS: Body mass index (BMI) and waist circumference (WC) are commonly used markers of cardiometabolic risk. However, sagittal abdominal diameter (SAD) has been proposed as a possibly more sensitive marker of intra-abdominal obesity. We investigated differences in how SAD, WC, and BMI were correlated with cardiometabolic risk markers. METHODS AND RESULTS: This cross-sectional study investigated anthropometric and metabolic baseline measurements of individuals from six trials. Multiple linear regression and (partial) correlation coefficients were used to investigate associations between SAD, WC, and BMI and cardiometabolic risk markers, including components of the metabolic syndrome as well as insulin resistance, blood lipids, and lowgrade inflammation. In total 1516 mostly overweight or obese individuals were included in the study. SAD was significantly more correlated with TG than WC for all studies, and overall increase in correlation was 0.05 (95% CI (0.02; 0.08). SAD was significantly more correlated with the markers TG and DBP 0.11 (95% CI (0.08, 0.14)) and 0.04 (95% CI (0.006, 0.07), respectively compared to BMI across all or most studies. CONCLUSION: This study showed that no single anthropometric indicator was consistently more strongly correlated across all markers of cardiometabolic risk. However, SAD was significantly more strongly correlated with TG than WC and significantly more strongly correlated with DBP and TG than BMI.

[52] *Djekic D, Shi L, Calais F et al.* **Effects of a Lacto-Ovo-Vegetarian Diet on the Plasma Lipidome and Its Association with Atherosclerotic Burden in Patients with Coronary Artery Disease-A Randomized, Open-Label, Cross-over Study**. Nutrients 2020; 12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33238431
ABSTRACT
A vegetarian diet has been associated with a lower risk of coronary artery disease (CAD). Plasma triacylglycerols, ceramides, and phosphatidylcholines may improve prediction of recurrent coronary events. We sought to investigate effects of a lacto-ovo-vegetarian diet (VD) on plasma lipidome in CAD patients and simultaneously assess associations of plasma lipids with the extent of coronary atherosclerotic burden. We analyzed 214 plasma lipids within glycerolipid, sphingolipid, and sterol lipid classes using lipidomics from a randomized controlled, crossover trial comprising 31 CAD patients on standard medical therapy. Subjects completed a four-week intervention with VD and isocaloric meat diet (MD), separated by a four-week washout period. The VD increased levels of 11 triacylglycerols and lowered 7 triacylglycerols, 21 glycerophospholipids, cholesteryl ester (18:0), and ceramide (d18:1/16:0) compared with MD. VD increased triacylglycerols with long-chain

polyunsaturated fatty acyls while decreased triacylglycerols with saturated fatty acyls, phosphatidylcholines, and sphingomyelins than MD. The Sullivan extent score (SES) exhibited on coronary angiograms were inversely associated with triacylglycerols with long-chain unsaturated fatty acyls. Phosphatidylcholines that were lower with VD were positively associated with SES and the total number of stenotic lesions. The VD favorably changed levels of several lipotoxic lipids that have previously been associated with increased risk of coronary events in CAD patients.

[53] *Mengel E, Bembi B, Del Toro M et al.* **Clinical disease progression and biomarkers in Niemann-Pick disease type C: a prospective cohort study**. Orphanet journal of rare diseases 2020; 15:328.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33228797

ABSTRACT

BACKGROUND: Niemann-Pick disease type C (NPC) is a rare, progressive, neurodegenerative disease associated with neurovisceral manifestations resulting from lysosomal dysfunction and aberrant lipid accumulation. A multicentre, prospective observational study (Clinical Trials.gov ID: NCT02435030) of individuals with genetically confirmed NPC1 or NPC2 receiving routine clinical care was conducted, to prospectively characterize and measure NPC disease progression and to investigate potential NPC-related biomarkers versus healthy individuals. Progression was measured using the abbreviated 5-domain NPC Clinical Severity Scale (NPCCSS), 17-domain NPCCSS and NPC clinical database (NPC-cdb) score. Cholesterol esterification and heat shock protein 70 (HSP70) levels were assessed from peripheral blood mononuclear cells (PBMCs), cholestane-3β,5α-,6β-triol (cholestane-triol) from serum, and unesterified cholesterol from both PBMCs and skin biopsy samples. The inter- and intra-rater reliability of the 5-domain NPCCSS was assessed by 13 expert clinicians' rating of four participants via video recordings, repeated after ≥3 weeks. Intraclass correlation coefficients (ICCs) were calculated. RESULTS: Of the 36 individuals with NPC (2-18 years) enrolled, 31 (86.1%) completed the 6-14-month observation period; 30/36 (83.3%) were receiving miglustat as part of routine clinical care. A mean (±SD) increase in 5-domain NPCCSS scores of 1.4 (±2.9) was observed, corresponding to an annualized progression rate of 1.5. On the 17-domain NPCCSS, a mean (±SD) progression of 2.7 (±4.0) was reported. Compared with healthy individuals, the NPC population had significantly lower levels of cholesterol esterification ($p<0.0001$), HSP70 ($p<0.0001$) and skin unesterified cholesterol ($p=0.0006$). Cholestane-triol levels were significantly higher in individuals with NPC versus healthy individuals ($p=0.008$) and correlated with the 5-domain NPCCSS (Spearman's correlation coefficient = 0.265, $p=0.0411$). The 5-domain NPCCSS showed high ICC agreement in inter-rater reliability (ICC = 0.995) and intra-rater reliability (ICC = 0.937). CONCLUSIONS: Progression rates observed were consistent with other reports on disease progression in NPC. The 5-domain NPCCSS reliability study supports its use as an abbreviated alternative to the 17-domain NPCCSS that focuses on the most relevant domains of the disease. The data support the use of cholestane-triol as a disease monitoring biomarker and the novel methods of measuring unesterified cholesterol could be applicable to support NPC diagnosis. Levels of HSP70 in individuals with NPC were significantly decreased compared with healthy individuals. TRIAL REGISTRATION: CT-ORZY-NPC-001: ClincalTrials.gov NCT02435030, Registered 6 May 2015, https://clinicaltrials.gov/ct2/show/NCT02435030 ; EudraCT 2014-005,194-37, Registered 28 April 2015, https://www.clinicaltrialsregister.eu/ctr-search/trial/2014-005194-37/DE . OR-REL-NPC-01: Unregistered.

[54] *Kong DX, Xiao YX, Zhang ZX, Liu YB*. **Study on the Correlation between Metabolism, Insulin Sensitivity and progressive weight loss change in Type-2 Diabetes**. Pak J Med Sci 2020; 36:1523-1528.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33235568

ABSTRACT
OBJECTIVE: To observe the changes of lipid metabolism, blood glucose level and insulin sensitivity in patients with Type-2 diabetes after progressive weight loss of their body weight, so as to lay a theoretical foundation for diabetes treatment and education in the future. METHODS: One hundred obese patients with Type-2 diabetes (BMI ≥ 25 kg/m(2)) who visited the endocrinology department of our hospital from April 2017 to April 2018 were given diabetes health education, diabetic diet, exercise and other measures to control their weight. The changes of blood glucose, blood lipid, insulin level and insulin release test before weight loss (T1), and at the time points of weight loss reached 5% (T2), 10% (T3) and 15% (T4) were recorded respectively to understand the influence of progressive weight loss on relevant indexes of patients. RESULTS: With the decrease of body weight, the differences of TC, TG, LDL-C and HDL-C at different weight loss points were significant ($p < 0.05$), and the changes of fasting blood glucose in 5% and 10% weight loss were significant ($p = 0.02$). The 2h postprandial blood glucose showed the most significant difference when the weight loss reached 15% ($p = 0.00$). There was no statistical difference in the change of glycosylated hemoglobin among different weight loss points ($p = 0.08$). When the weight loss reached 10%, the blood insulin level was significantly lower than that before the weight loss, while the insulin level was not significantly changed when the weight loss reached 15%, but the peak of secretion was shifted forward. It is suggested that insulin sensitivity gradually increases with weight loss. CONCLUSION: Obese patients with Type-2 diabetes can benefit from weight loss, with abnormal blood glucose and lipid metabolism improved, insulin resistance relieved, and insulin sensitivity increased.

[55] *Xu XD, Han X, Yang Y, Li X*. **Comparative study on the efficacy of peritoneal dialysis and hemodialysis in patients with end-stage diabetic nephropathy**. Pak J Med Sci 2020; 36:1484-1489.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33235561

ABSTRACT
OBJECTIVE: Diabetic nephropathy is a serious threat to human health, and its incidence is on the rise. End-stage diabetic nephropathy (ESDN) requires extra investigation due to its complexity and severity, as well as serious concurrent diseases. Our objective was to compare the efficacy of hemodialysis (HD) and peritoneal dialysis (PD) in the treatment of ESDN. METHODS: Clinical data of 84 patients with ESDN admitted to our hospital from June 2016 to June 2018 were retrospectively analyzed. The patients were divided into an HD group that received hemodialysis and a PD group that received peritoneal dialysis. Their general conditions, biochemical indicators, residual renal function and incidence of complications were recorded and compared between the two groups. RESULTS: (1) No significant difference in diastolic blood pressure, systolic blood pressure, body weight, or urine output was detected between the two groups at the beginning of dialysis ($P>0.05$). (2) Compared to the PD group, the HD group had significantly lower total cholesterol (TC) and triglyceride (TG) ($P<0.05$), and significantly higher total protein (TP) and albumin (ALB) after treatment ($P<0.05$). (3) The two groups also showed significant difference in residual renal function

after treatment (P<0.05). (4) The HD group had significantly higher systolic pressure than the PD group after treatment (P<0.05). And more cases of infection were observed in the PD group than the HD group (P<0.05). CONCLUSION: Both HD and PD are used for treatment of ESDN, and can achieve similar calcium and phosphorus control. Compared to HD, PD has less adverse effect on hemodynamics and better preserves residual renal function, but is more likely to cause malnutrition and disorders of lipid metabolism. Therefore, choice of dialysis method should be based on specific conditions of each patient.

[56] *Soares IP, Oliveira BAC, Baal SCS et al.* **Fish oil supplementation enhances colon recovery after experimental colitis**. Prostaglandins, leukotrienes, and essential fatty acids 2020; 163:102212.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33249348
ABSTRACT
INTRODUCTION: Fish oil (FO) has an anti-inflammatory and pro-resolution activity and it has been used to restore physiological disturbances on inflammatory conditions. Here, we investigate whether FO supplementation could, acutely, prevent or restore inflammatory damages on experimental colitis. METHODS: Wistar rats orally received 2 g.kg(-1).day(-1) of FO for 30 days before induction of experimental colitis. Specimens were collected on the 2nd and 7th days after colitis-induction and intestinal mucus, inflammatory activity and colon integrity were determined. RESULTS: Experimental colitis did cause colon disruption and FO, acutely, did not prevent the loss of intestinal and fecal mucus, neither the increase of inflammatory activity and intestinal permeability. On the 7th day of colitis, FO soften the perturbations of experimental colitis, increasing histological and fecal mucus and, also decreased inflammatory activity, but this was not accompanied by intestinal permeability. CONCLUSION: FO did not protect, acutely, intestinal damages from experimental colitis, but at long run promotes higher intestinal recovery.

[57] *Palma Sobrinho ND, Campos JF, Silva RCD*. **Adverse drug reactions related to potential serious drug interactions in patients with cardiovascular diseases**. Rev Gaucha Enferm 2020; 41:e20190511.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33237225
ABSTRACT
OBJECTIVE: To assess the occurrence of adverse drug reactions associated with potential serious drug interactions identified in prescriptions of hospitalized patients with cardiovascular disease. METHOD: A documentary, quantitative, and cross-sectional research study. Between August and September 2016, ninety-nine prescriptions of patients hospitalized for more than 48 hours in the cardiology ward of a hospital in Rio de Janeiro were analyzed. Drug interactions were evaluated by Micromedex®, and adverse events were identified through trackers and analyzed by specialists using the Naranjo Algorithm, by means of descriptive statistics. RESULTS: Eighteen potential serious interactions were detected in 22 drug pairs, mainly simvastatin x anlodipine (18%) and enoxaparin x clopidogrel (18%). Of the 18 medical records investigated, four trackers were found and three probable adverse events (16.6%) were defined due to hemorrhagic changes in patients. CONCLUSION: Drug interactions are likely to cause harm to the patient, which requires implementing barriers for the safety of the medication system.

[58] *Luo S, You XB, Liu Q*. **[Effects of Atorvastatin Calcium on the Survival of Ultra-long Dorsal Random Skin Flaps in Rats]**. Sichuan Da Xue Xue Bao Yi Xue Ban 2020; 51:803-808.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33236604

ABSTRACT

OBJECTIVE: To investigate the effects of atorvastatin calcium (ATR) on the survival of ultra-long dorsal random skin flaps in rats. METHODS: Thirty SD rats were divided into five groups (n=6) according to the random number table: normal saline control group (CON group), ATR 10 mg/kg group (P10 group), ATR 20 mg/kg group (P20 group), ATR 30 mg/kg group (P30 group), and ATR 40 mg/kg group (P40 group). After pretreatment with ATR or 0.9% saline for 3 days, an ultra-long dorsal random skin flaps with size of 8 cm×2 cm was made on the back of each rat and replanted in situ. After the operation, the ATR or saline treatment lasted for 3 d. Seven days after operation, the appearance of skin flaps was observed with naked eyes, the survival rate of skin flaps was calculated. The pathological changes in the surviving areas of skin flaps were observed by HE staining, the number of microvessels in skin flaps was observed by immunohistochemistry staining, the mRNA expressions of vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) were tested by quantitative real-time PCR, and the contents of superoxide dismutase, nitrogen monoxide and malonaldehyde were tested by enzyme linked immunosorbent assays (ELISA). RESULTS: On the 7 (th)day after operation, the skin flap of the CON group showed a large area of necrosis, and the necrotic part formed crusts. Crusts were hard and inelastic, and a large amount of tissue fluid exudated. The fascial layer showed dark purple. No exudation of tissue fluid was observed in the flaps of P10, P20, P30 and P40 groups. The scab shell fell off naturally and the fur grew normally. HE staining of CON group showed that a large number of inflammatory cell infiltration, epidermal loss and necrosis in skin flaps, but the pathological changes in skin flaps were significantly improved after treatment with ATR. Compared with the CON group, the survival rate of skin flaps, the number of microvessels in skin flaps and the levels of VEGF mRNA, bFGF mRNA, SOD, NO in skin flaps also increased with the dose of ATR, which reached a peak at 30 mg/kg ATR ($P<0.05$). However, the level of MDA in skin flaps decreased with the dose of ATR, which reached the lowest at 30 mg/kg ATR ($P<0.05$). CONCLUSION: ATR can enhance the survival of ultra-long dorsal random skin flaps in rats, which may be related to promoting microangiogenesis and inhibiting inflammatory and oxidative stress.

[59] *Emamat H, Zahedmehr A, Asadian S et al.* **Effect of barberry (Berberis vulgaris) consumption on blood pressure, plasma lipids, and inflammation in patients with hypertension and other cardiovascular risk factors: study protocol for a randomized clinical trial**. Trials 2020; 21:986.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33246500

ABSTRACT

BACKGROUND: Cardiovascular diseases (CVDs) remain the leading causes of morbidity and mortality in the world. Hypertension is an important and prevalent cardiovascular risk factor. The present study will be conducted to investigate the effect of barberry as a cardio-protective fruit on the blood pressure in patients with hypertension and other CVD risk factors. Furthermore, plasma concentrations of lipids and inflammatory biomarkers will be evaluated. METHODS/DESIGN: This is an 8-week, prospective, single-blinded, parallel assigned, randomized controlled clinical trial (RCT) in which eligible men and women with hypertension and other cardiovascular risk factors will be

randomized to either placebo powder (PP; containing 9 g maltodextrin, 1 g citric acid, 1 g milled sucrose and edible red color (n = 37)) or barberry powder (BP; containing 10 g milled dried barberry and 1 g of milled sucrose (n = 37)) groups. At baseline and after 8 weeks of intervention, plasma lipids and inflammatory markers, 24-h urinary nitrite/nitrate and sodium excretion, and 24-h ambulatory blood pressure monitoring (ABPM) will be measured. Anthropometric measures and dietary assessment will be performed as well. Data analysis will be done using SPSS version-21 software. DISCUSSION: The interest in natural and functional food products has increased globally. This RCT will add to the growing literature for the potential antihypertensive, lipid-lowering, and anti-inflammatory effects of barberry in humans. TRIAL REGISTRATION: ClinicalTrials.gov (NCT number) NCT04084847 . Registered on 10 December 2019.

[60] *Lerner D, Garvey K, Arrighi-Allisan A et al.* **Letter to the editor: Study Summary - Randomized Control Trial of Omega-3 Fatty Acid Supplementation for the Treatment of COVID-19 Related Olfactory Dysfunction**. Trials 2020; 21:942.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33225989
ABSTRACT
OBJECTIVES: To evaluate a therapeutic role for omega-3 fatty acid supplementation in the treatment of olfactory dysfunction associated with COVID-19 infection TRIAL DESIGN: Randomized, double-blinded, placebo-controlled trial PARTICIPANTS: Eligible patients are adults with self-reported new-onset olfactory dysfunction of any duration associated with laboratory-confirmed or clinically suspected COVID-19 patients. Exclusion criteria include patients with pre-existing olfactory dysfunction, history of chronic rhinosinusitis or history of sinus surgery, current use of nasal steroid sprays or omega-3 supplementation, fish allergy, or inability to provide informed consent for any reason. The trial is conducted at Mount Sinai Hospital INTERVENTION AND COMPARATOR: The intervention group will receive 2000 mg daily of omega-3 supplementation in the form of two "Fish Oil, Ultra Omega-3" capsules (product of Pharmavite®) daily. The comparator group will take 2 placebo capsules of identical size, shape, and odor daily for 6 weeks. MAIN OUTCOMES: Each subject will take a Brief Smell Identification Test at study enrolment and completion after 6 weeks. The primary outcome will be change in Brief Smell Identification Test over the 6-week period. RANDOMISATION: Patients will be randomized by the Investigational Drug Pharmacy at the Icahn School of Medicine at Sinai via a computer-generated sequence in a 1:1 allocation to treatment or control arms. BLINDING (MASKING): Both participants and researchers will be blinded. NUMBERS TO BE RANDOMISED (SAMPLE SIZE): There will be 88 participants randomized to each group. A total of 176 participants will be randomized. TRIAL STATUS: Protocol Version 1, 8/3/2020 Recruitment is ongoing, started 8/5/2020 with estimated completion 11/30/2020. TRIAL REGISTRATION: The trial is registered on ClinicalTrials.gov with Protocol Identifier: NCT04495816 . TRIAL REGISTRATION: ClinicalTrials.gov, NCT04495816 . Registered 3 August 2020 FULL PROTOCOL: The full protocol is attached as an additional file, accessible from the Trials website (Additional file 1).

[61] *Jurisic A, Jurisic Z, Lefkou E, Girardi G*. **Pravastatin plus L-arginine prevents adverse pregnancy outcomes in women with uteroplacental vascular dysfunction**. Vascular pharmacology 2020:106824.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33249273
ABSTRACT

BACKGROUND: Uteroplacental vascular dysfunction, characterized by diminished uterine artery (UtA) blood flow in the second trimester is a clinically useful predictor of the further development of preeclampsia, fetal growth restriction and stillbirth. Efforts to develop effective treatments to protect pregnancies with abnormal UtA Dopplers would be of significant clinical benefit for mothers and their fetuses. OBJECTIVE: The aim of this pilot non randomized control study was to use pravastatin +L-arginine to improve uteroplacental haemodynamics and prevent adverse maternal and neonatal outcomes in women with abnormal Dopplers and high risk for developing adverse pregnancy outcomes. STUDY DESIGN: This study was performed between 2015 and 2018. All women received primary care at OB/GYN Polyclinic Jurisic and Narodni Front University Hospital, University of Belgrade Medical School, Serbia. Approval for investigational drug use was obtained and all women gave informed consent. 10 pregnant women with a poor obstetric history that developed uteroplacental dysfunction (UtA pulsatility index (PI) above the 95th percentile and notching) at 20.5 weeks IQR [17.7-22] gave consent to be treated daily with pravastatin (40 mg) and L-arginine (1.5 g) to improve placental blood flow and pregnancy outcomes. 5 women remained untreated after diagnosis at 21 weeks [20-22] (control group). Due to presence of risk factors for pregnancy complications, close maternal and fetal monitoring was undertaken in all patients. Doppler examinations were performed to monitor changes in placental vascular resistance and fetal well-being and growth. RESULTS: PRAV+L-arginine improved uteroplacental haemodynamics, increased fetal growth and prevented early onset preeclampsia leading to delivery close to term (delivery date: median 38 weeks, IQR[36.5-39]) and appropriate weight for gestational age compared to controls, in which placental blood flow did not improve and 2 women developed severe early onset preeclampsia. Neonates from the control group were born preterm (25 weeks IQR[23.5-25]), growth restricted and spent several months at NICU. Two neonates died due to prematurity-associated complications. PRAV+L-arginine treatment prolonged pregnancies for 4.1 months, compared to 26 days in the untreated group, preventing neonatal complications associated with prematurity. The infants are now 1-3 years old and show normal growth and development. CONCLUSION: This study describes the successful management with pravastatin+L-arginine of 10 pregnant patients with uteroplacental vascular dysfunction and high risk of adverse maternal and fetal outcomes. A larger study is being organized to confirm these observations.

[62] *Chello C, Nenna A, Chello M et al.* **Statin treatment and hypertrophic scarring after cardiac surgery**. Wound Repair Regen 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33236817

ABSTRACT

Wound healing process after surgical procedure plays a crucial role to prevent blood loss and infections. Hypertrophic scars might occur after surgery and are generally associated with an inflammatory burden. Cardiac surgery is intrinsically related to a strong systemic inflammatory state that might favor hypertrophic scarring. Besides lipid-lowering effects, statins are known for their pleiotropic and anti-inflammatory activity. The aim of this study was to investigate the impact of statins in the healing process after median sternotomy in patients undergoing cardiac surgery. All patients undergoing major cardiac surgery with median sternotomy and cardiopulmonary bypass, and subsequently evaluated in the outpatient clinic after discharge, were included in this study. A total of 930 Caucasian patients were retrospectively reviewed. At outpatient visit, 276 patients (29.7%) showed the formation of hypertrophic scars. Patients with hypertrophic scars tended to be younger

(P=0.001) and non-statin users (P=0.001). Logistic regression analysis confirmed the protective role of statins (odds ratio 0.39, 95% confidence interval 0.29-0.53, P=0.001), after adjustment for age. A dose-dependent effect was confirmed, showing a more intensive protective effect for higher doses of statins. Statin use might be correlated with reduced hypertrophic scars after cardiac surgery through median sternotomy. A dose-dependent effect has been shown, and statin effect seems to be independent of age in a selected population undergoing surgery with an elevated inflammatory burden. Although further studies are warranted to elucidate the biologic mechanisms, the concept of using statins as anti-scarring agents is novel and should be investigated with tailored studies.

[63] *Wu YX, Wang Y*. **[Progress on the molecular mechanisms of PCSK9-mediated degradation of low density lipoprotein receptor]**. Yi Chuan 2020; 42:965-978.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33229322

ABSTRACT

Elevated serum level of low density lipoprotein cholesterol (LDL-C) is the leading risk factor for cardiovascular disease. LDL receptor (LDLR)-mediated LDL clearance is the major factor determining the LDL-C level in the circulation. LDL binds to the LDLR on the cell surface and enters the cells through classical clathrin-coated vesicles. In the acidic endosome, LDLR is uncoupled from LDL and recycles back to the cell surface. The released LDL is transported to the lysosome for degradation. The proprotein convertase subtilisin kexin type 9 (PCSK9) gene encodes a hepatic secretory protein, and its mutations are strongly associated with levels of LDL-C. We and others have shown that PCSK9 directly interacts with LDLR on the cell surface and both are internalized through the clathrin-coated vesicles. However, in the acidic endosome, PCSK9 and LDLR form a tight complex and are targeted to lysosome for degradation, thereby reducing the level of LDLR on the surface of hepatocytes and decreasing hepatic clearance of LDL-C, which plays an important role in maintaining a relatively constant level of LDL in the plasma. Thus, blocking PCSK9 function has become a new strategy to treat hypercholesterolemia.In this review, we will summarize the latest progress in the functional and mechanistic studies of PCSK9 and also highlight the research progress of PCSK9 inhibitors. It aims to provide a reference for the study of PCSK9-LDLR pathway and the regulation of cholesterol metabolism.