[1] *Luan Y, Wang M, Zhao L et al.* **Safety and Efficacy of Perioperative Use of Evolocumab in Myocardial Infarction Patients: Study Protocol for a Multicentre Randomized Controlled Trial**. Adv Ther 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33638801

ABSTRACT

INTRODUCTION: The SECURE-PCI study supports a perioperative loading dose of statins, although whether an intensive lipid-lowering strategy prior to percutaneous coronary intervention further benefits acute coronary syndrome patients remains controversial. Evolocumab, a proprotein-converting enzyme subtilisin/kexin type 9 (PCSK9) inhibitor, acts more quickly and effectively than statins and reduces the risk of cardiovascular events in post-myocardial infarction (MI) patients. Nonetheless, whether it can be safely used in perioperative MI patients and whether perioperative application can benefit patients are still unknown. This study aims to evaluate the safety and efficacy of this treatment regimen. METHODS: A multicentre, prospective, randomized, controlled superiority trial will be conducted in 530 statin-naïve MI patients. All eligible patients will be randomized to the evolocumab group (140 mg subcutaneously injected once before revascularization + 14 days after the first dose) or the control group (no evolocumab injection). Evolocumab will then be administered depending on the patient's lipid profile. Both groups will be treated simultaneously with standardized secondary preventive medications. The primary end points are major adverse cardiovascular events (a composite of death, recurrent MI, unanticipated revascularization, stroke and any rehospitalization for ischaemic causes) within 12 months. The secondary end point is post-infarction angina after pain relief. The safety end points include myopathy, impaired liver or renal function, and other adverse events during the follow-up period. OUTCOMES: This is the first trial to evaluate the safety and efficacy of evolocumab pre-treatment on prognosis in MI patients. Perioperative evolocumab injection may be a new, safe way to improve prognosis. TRIAL REGISTRATION: Chinese Clinical Trial Registry (http://www.chictr.org.cn ; ChiCTR1900024526). Registered on 13 July 2019 and updated on 31 May 2020. The study is currently recruiting patients.

[2] *Xie H, Min M, Guo S et al.* **Impact of Vitamin D and Vitamin D Receptor on Risk of Cardiovascular Diseases in Children and Adolescents with Obesity in Sichuan, China: A Cross-Sectional Study**. Annals of nutrition & metabolism 2021:1-9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33626539

ABSTRACT

BACKGROUND: Previous studies have demonstrated the close relationship between vitamin D, vitamin D receptor (VDR), and obesity. Nevertheless, few studies have reported wherther the relationship among these is associated with the risk of cardiovascular diseases (CVDs) in Chinese children and adolescents. OBJECTIVE: The present study aimed to reveal the effects of obesity, serum vitamin D levels, and VDR FokI genotype on the risk of CVDs in children and adolescents in Sichuan, China. METHODS: Children and adolescents were recruited into a cross-sectional study. Serum vitamin D levels, serum lipid levels, and VDR FokI gene polymorphisms were measured in the laboratory. The selected lipid factors were used as biomarkers of CVD risk. The impact of obesity, vitamin D levels and VDR FokI genotype on CVD risk factors were investigated. RESULTS: Higher lipid levels were observed in children and adolescents in the obese group, when compared to the nonobese group. In the obese group, the C allele carriers had significantly lower concentrations of lipids, when compared to the TT genotype. C allele carriers who were vitamin D deficient had lower

levels of total cholesterol (TC), triglycerides (TG), apolipoprotein B (Apo-B), total cholesterol/high-density lipoprotein cholesterol (TC/HDL-C), low-density lipoprotein cholesterol/high-density lipoprotein cholesterol (LDL-C/HDL-C), and triglycerides/high-density lipoprotein cholesterol (TG/HDL-C), when compared to those with the TT genotype in obese children and adolescents. For vitamin D-insufficient obese children and adolescents, the TC, Apo-B, and TC/HDL-C in the C allele carriers were significantly lower, when compared to those in the TT genotype in obese children and adolescents. CONCLUSION: Obese children with low vitamin D levels, who are carriers of the C allele of the FokI gene, have lower levels of several biochemical markers of CVD risk, when compared to those who were TT homozygous. Obese children and adolescents may benefit from vitamin D supplementation, terms of lowering their CVD risk, particularly when they are carriers of the C allele of the FokI gene.

[3] *Ferraz-Amaro I, Delgado-Frías E, Hernández-Hernández V et al.* **HDL cholesterol efflux capacity and lipid profile in patients with systemic sclerosis**. Arthritis research & therapy 2021; 23:62.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33622410
ABSTRACT
OBJECTIVE: It is well established that patients with systemic sclerosis (SSc) have a disrupted lipid profile and an increased cardiovascular risk. Cholesterol efflux capacity (CEC), the ability of high-density lipoprotein (HDL)-cholesterol to accept cholesterol from macrophages, has been linked to cardiovascular events. The aim of this study was to establish whether CEC and lipid profile were impaired in SSc patients with respect to controls and whether these changes were associated with disease-related data. METHODS: Cross-sectional study encompassed 188 individuals: 73 SSc patients and 115 controls. CEC, using an in vitro assay, and lipoprotein serum concentrations were assessed in patients and controls. A multivariable analysis was performed to study the differences in CEC between patients and controls, and if SSc-related data could explain such differences. RESULTS: The multivariable analysis adjusted for demographic characteristics, cardiovascular risk factors, and lipid-related molecules showed that total cholesterol (beta coefficient: -22 [95%CI - 37 to - 7], p = 0.004), triglycerides (beta coefficient: 24 [95%CI 2-47], p = 0.033), lipoprotein A (beta coefficient: 22 [95%CI 2-43], p = 0.033), and CEC (beta coefficient: - 6 [95%CI - 10 to - 2]%,p = 0.002) were significantly different between patients and controls. Skin thickness, as assessed by modified Rodnan skin score, was independently associated with a lower CEC (beta coefficient: - 0.21 [95%CI - 0.37 to - 0.05]%, p = 0.011) after multivariable adjustment. CONCLUSION: SSc patients show an abnormal lipid profile with respect to controls including CEC. Skin thickness is independent and inversely associated with CEC in SSc patients.

[4] *Weber B, He Z, Yang N et al.* **Divergence of Cardiovascular Biomarkers of Lipids and Subclinical Myocardial Injury Among Rheumatoid Arthritis Patients with Increased Inflammation**. Arthritis & rheumatology (Hoboken, N.J.) 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33615723
ABSTRACT
BACKGROUND: Patients with rheumatoid arthritis (RA) have a 1.5x excess risk of cardiovascular (CV) disease attributed to chronic inflammation. A decrease in inflammation in RA is associated with increased LDL-C. This study evaluated the changes in lipid levels prospectively among RA patients experiencing changes in inflammation and determined the association with concomitant temporal

patterns in markers of myocardial injury. METHODS: We studied 196 patients in a longitudinal RA cohort with blood samples and hsCRP measured annually, who experienced either a significant increase or decrease in inflammation, defined as hsCRP ≥10 mg/L, in 2 consecutive annual visits. Routine and advanced lipids, markers of inflammation (IL-6, hsCRP, sTNFR2), and markers of subclinical myocardial injury (hs-cTnT, NT-proBNP) were measured RESULTS: The mean age was 59 years, 81% female, with mean RA disease duration of 17.9 years. The average hsCRP increase was 36 mg/dl, associated with significant reductions in LDL-C, TG, TC, apoB and apoA1. At baseline in the increase cohort, 45.6% (47/103) had detectable circulating hs-cTnT which further increased during inflammation (p=0.02). In the decrease cohort, hs-cTnT levels remained stable despite a reduction in inflammation. In both cohorts, levels of hs-cTnT associated with overall estimated cardiovascular risk. CONCLUSION: Among RA patients experiencing an increase in inflammation, routine lipids, including LDL-C, were significantly decreased while increases in markers of subclinical myocardial injury were observed. These findings highlight the divergence in biomarkers of CV risk and suggest a role in future studies examining the utility of including hs-cTnT for CV risk stratification in RA.

[5] *Rivera K, Quiñones V, Amigo L et al.* **Lipoprotein receptor SR-B1 deficiency enhances adipose tissue inflammation and reduces susceptibility to hepatic steatosis during diet-induced obesity in mice**. Biochimica et biophysica acta. Molecular and cell biology of lipids 2021:158909.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33631309
ABSTRACT
Scavenger receptor class B type 1 (SR-B1) is a membrane lipoprotein receptor/lipid transporter involved in the pathogenesis of atherosclerosis, but its role in obesity and fatty liver development is unclear. Here, we determined the effects of SR-B1 deficiency on plasma metabolic and inflammatory parameters as well as fat deposition in adipose tissue and liver during obesity. To induce obesity, we performed high-fat diet (HFD) exposure for 12 weeks in male SR-B1 knock-out (SR-B1(-/-), n = 14) and wild-type (WT, n = 12) mice. Compared to HFD-fed WT mice, plasma from HFD-fed SR-B1(-/-) animals exhibited increased total cholesterol, triglycerides (TG) and TNF-α levels. In addition, hypertrophied adipocytes and macrophage-containing crown-like structures (CLS) were observed in adipose tissue from HFD-fed SR-B1 deficient mice. Remarkably, liver from obese SR-B1(-/-) mice showed attenuated TG content, dysregulation in hepatic peroxisome proliferator-activated receptors (PPARs) expression, increased hepatic TG secretion, and altered hepatic fatty acid (FA) composition. In conclusion, we show that SR-B1 deficiency alters the metabolic environment of obese mice through modulation of liver and adipose tissue lipid accumulation. Our findings provide the basis for further elucidation of SR-B1's role in obesity and fatty liver, two major public health issues that increase the risk of advanced chronic diseases and overall mortality.

[6] *Beddhu S, Boucher RE, Sun J et al.* **Chronic kidney disease, atherosclerotic plaque characteristics on carotid magnetic resonance imaging, and cardiovascular outcomes**. BMC Nephrol 2021; 22:69.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33627066
ABSTRACT

BACKGROUND: It is unclear whether faster progression of atherosclerosis explains the higher risk of cardiovascular events in CKD. The objectives of this study were to 1. Characterize the associations of CKD with presence and morphology of atherosclerotic plaques on carotid magnetic resonance imaging (MRI) and 2. Examine the associations of baseline CKD and carotid atherosclerotic plaques with subsequent cardiovascular events. METHODS: In a subgroup (N = 465) of Systolic Blood Pressure Intervention Trial. (SPRINT) participants, we measured carotid plaque presence and morphology at baseline and after 30-months with MRI. We examined the associations of CKD (baseline eGFR < 60 ml/min/1.73m(2)) with progression of carotid plaques and the SPRINT cardiovascular endpoint. RESULTS: One hundred and ninety six (42%) participants had CKD. Baseline eGFR in the non-CKD and CKD subgroups were 77 ± 14 and 49 ± 8 ml/min/1.73 m(2), respectively. Lipid rich necrotic-core plaque was present in 137 (29.5%) participants. In 323 participants with both baseline and follow-up MRI measurements of maximum wall thickness, CKD was not associated with progression of maximum wall thickness (OR 0.62, 95% CI 0.36 to 1.07, p = 0.082). In 96 participants with necrotic core plaque at baseline and with a valid follow-up MRI, CKD was associated with lower odds of progression of necrotic core plaque (OR 0.41, 95% CI 0.17 to 0.95, p = 0.039). There were 28 cardiovascular events over 1764 person-years of follow-up. In separate Cox models, necrotic core plaque (HR 2.59, 95% CI 1.15 to 5.85) but not plaque defined by maximum wall thickness or presence of a plaque component (HR 1.79, 95% CI 0.73 to 4.43) was associated with cardiovascular events. Independent of necrotic core plaque, CKD (HR 3.35, 95% CI 1.40 to 7.99) was associated with cardiovascular events. CONCLUSIONS: Presence of necrotic core in carotid plaque rather than the presence of plaque per se was associated with increased risk of cardiovascular events. We did not find CKD to be associated with faster progression of necrotic core plaques, although both were independently associated with cardiovascular events. Thus, CKD may contribute to cardiovascular disease principally via mechanisms other than atherosclerosis such as arterial media calcification or stiffening. TRIAL REGISTRATION: NCT01475747 , registered on November 21, 2011.

[7] *Herrett E, Williamson E, Brack K et al.* **Statin treatment and muscle symptoms: series of randomised, placebo controlled n-of-1 trials**. Bmj 2021; 372:n135.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33627334

ABSTRACT

OBJECTIVE: To establish the effect of statins on muscle symptoms in people who had previously reported muscle symptoms when taking statins. DESIGN: Series of randomised, placebo controlled n-of-1 trials. SETTING: Primary care across 50 sites in the United Kingdom, December 2016 to April 2018. PARTICIPANTS: 200 participants who had recently stopped or were considering stopping treatment with statins because of muscle symptoms. INTERVENTIONS: Participants were randomised to a sequence of six double blinded treatment periods (two months each) of atorvastatin 20 mg daily or placebo. MAIN OUTCOME MEASURES: At the end of each treatment period, participants rated their muscle symptoms on a visual analogue scale (0-10). The primary analysis compared symptom scores in the statin and placebo periods. RESULTS: 151 participants provided symptoms scores for at least one statin period and one placebo period and were included in the primary analysis. Overall, no difference in muscle symptom scores was found between the statin and placebo periods (mean difference statin minus placebo -0.11, 95% confidence interval -0.36 to 0.14; P=0.40)). Withdrawals because of intolerable muscle symptoms were 18 participants (9%) during a

statin period and 13 (7%) during a placebo period. Two thirds of those completing the trial reported restarting long term treatment with statins. CONCLUSIONS: No overall effect of atorvastatin 20 mg on muscle symptoms compared with placebo was found in participants who had previously reported severe muscle symptoms when taking statins. Most people completing the trial intended to restart treatment with statins. N-of-1 trials can assess drug effects at the group level and guide individual treatment. TRIAL REGISTRATION: ISRCTN30952488, EUDRACT 2016-000141-31, NCT02781064.

[8] *Collard D, Nurmohamed NS, Kaiser Y et al.* **Cardiovascular risk factors and COVID-19 outcomes in hospitalised patients: a prospective cohort study**. BMJ open 2021; 11:e045482.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33619201

ABSTRACT

OBJECTIVES: Recent reports suggest a high prevalence of hypertension and diabetes in COVID-19 patients, but the role of cardiovascular disease (CVD) risk factors in the clinical course of COVID-19 is unknown. We evaluated the time-to-event relationship between hypertension, dyslipidaemia, diabetes and COVID-19 outcomes. DESIGN: We analysed data from the prospective Dutch CovidPredict cohort, an ongoing prospective study of patients admitted for COVID-19 infection. SETTING: Patients from eight participating hospitals, including two university hospitals from the CovidPredict cohort were included. PARTICIPANTS: Admitted, adult patients with a positive COVID-19 PCR or high suspicion based on CT-imaging of the thorax. Patients were followed for major outcomes during the hospitalisation. CVD risk factors were established via home medication lists and divided in antihypertensives, lipid-lowering therapy and antidiabetics. PRIMARY AND SECONDARY OUTCOMES MEASURES: The primary outcome was mortality during the first 21 days following admission, secondary outcomes consisted of intensive care unit (ICU) admission and ICU mortality. Kaplan-Meier and Cox regression analyses were used to determine the association with CVD risk factors. RESULTS: We included 1604 patients with a mean age of 66±15 of whom 60.5% were men. Antihypertensives, lipid-lowering therapy and antidiabetics were used by 45%, 34.7% and 22.1% of patients. After 21-days of follow-up; 19.2% of the patients had died or were discharged for palliative care. Cox regression analysis after adjustment for age and sex showed that the presence of ≥2 risk factors was associated with increased mortality risk (HR 1.52, 95% CI 1.15 to 2.02), but not with ICU admission. Moreover, the use of ≥2 antidiabetics and ≥2 antihypertensives was associated with mortality independent of age and sex with HRs of, respectively, 2.09 (95% CI 1.55 to 2.80) and 1.46 (95% CI 1.11 to 1.91). CONCLUSIONS: The accumulation of hypertension, dyslipidaemia and diabetes leads to a stepwise increased risk for short-term mortality in hospitalised COVID-19 patients independent of age and sex. Further studies investigating how these risk factors disproportionately affect COVID-19 patients are warranted.

[9] *Ameri P, Tini G, Spallarossa P et al.* **Cardiovascular safety of the tyrosine kinase inhibitor nintedanib**. British journal of clinical pharmacology 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33620103

ABSTRACT

The intracellular tyrosine kinase inhibitor nintedanib has shown great efficacy for the treatment of idiopathic pulmonary fibrosis (IPF) and other interstitial lung diseases. However, the incidence rate of myocardial infarction (MI) among participants in landmark IPF trials was remarkable, peaking at 3/100 patients-year. Although subjects with IPF often have a high cardiovascular (CV) risk profile, the

occurrence of MI in nintedanib-treated patients may not be fully explained by clustering of CV risk factors. Nintedanib inhibits the vascular endothelial growth factor, platelet-derived growth factor and fibroblast growth factor pathways, which play important roles in the biology of the atherosclerotic plaque and in the response of the heart to ischemia. Hence, unwanted CV effects may partly account for nintedanib-related MI. We review the evidence supporting this hypothesis and discuss possible actions for a safe implementation of nintedanib in clinical practice, building on the experience with tyrosine kinase inhibitors acquired in cardio-oncology.

[10] *Badimon L*. **New trials in the scene of cardiovascular disease at AHA 2020: innovation, controversy, and reassurance**. Cardiovascular research 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33615348
ABSTRACT

[11] *Feng S, Wang L, Shao P et al.* **A review on chemical and physical modifications of phytosterols and their influence on bioavailability and safety**. Critical reviews in food science and nutrition 2021:1-20.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33612007
ABSTRACT
Phytosterols have been shown to lower cholesterol levels and to have antioxidant, anti-inflammatory and other biological activities. However, the high melting point and poor solubility limit their bioavailability and practical application. It is advantageous to modify phytosterols chemically and physically. This article reviews and discusses the chemical and physical modifications of phytosterols, as well as their effects on the bioavailability and possible toxicity in vivo. The current research on chemical modifications is mainly focused on esterification to increase the oil solubility and water solubility. For physical modifications (mainly microencapsulation), there are biopolymer-based, surfactant-based and lipid-based nanocarriers. Both chemical and physical modifications of phytosterols can effectively increase the absorption and bioavailability. The safety of modified phytosterols is also an important issue. Phytosterol esters are generally considered to be safe. However, phytosterol oxides, which may be produced during the synthesis of phytosterol esters, have shown toxicity in animal models. The toxicity of nanocarriers also needs further studies.

[12] *Kumar S, Khurana NK, Awan I et al.* **The Effect of Preoperative Hematocrit Levels on Early Outcomes After Coronary Artery Bypass Graft**. Cureus 2021; 13:e12733.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33614335
ABSTRACT
Introduction Coronary artery bypass graft (CABG) is the most potent of surgical procedures; in this procedure, the narrowing of the coronary artery due to atherosclerotic plaque is bypassed by forming an alternate route for blood flow to the heart. There are various risk factors associated with the procedure. The aim of this study was to observe if postoperative outcomes are affected by preoperative hematocrit (hct) levels in patients. Methods This longitudinal study was conducted from April 2019 to December 2019. Eighty-two (82) participants who were to undergo CABG surgery were divided into two groups based on their preoperative hct levels. Group 1 had 42 participants with lower levels of hct (less than 35.5% for women and 38.3% for men), whereas group 2 consisted of 40 participants with normal hct levels (greater than 35.5% for women and 38.3% for men). Results The

results showed that participants undergoing CABG with lower than normal hct levels had increased blood loss through drainage as compared to participants who had normal hct levels (680.1 ± 301 mL vs. 500.7 ± 412 mL; p-value: 0.02). Group 1 participants also had an increased need for blood and blood product transfusion as compared to group 2 (3.2 ± 1.8 units vs. 1.8 ± 0.9 units; p-value: <0.0001). Furthermore, the participants in group 1 had longer stays in the ICU relative to the other group (5.2 ± 3.1 days vs. 3.4 ± 2.5 days; p-value: 0.003). Conclusion Based on our findings, patients who undergo CABG surgery with lower than normal hct levels are at increased risk of certain complications, including excessive blood loss, need for transfusion, and increased duration of ICU stay. Therefore, preoperative hct levels should be routinely checked in patients undergoing CABG to prevent these complications.

[13] *Toulassi IA, Al Saedi UA, Gutlapalli SD et al.* **A Paradigm Shift in the Management of Atherosclerosis: Protective Role of Sirtuins in Atherosclerosis**. Cureus 2021; 13:e12735.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33614337

ABSTRACT

Facing the rise of an aging population and age-related pathologies such as atherosclerosis will continue to be some of the biggest challenges encountering health care. Regardless of considerable advancements in management and prevention to deal with atherosclerosis and other related pathologies. The current guidelines for preventing and managing atherosclerotic diseases are lifestyle changes, blood pressure control, blood glucose control, and lipid control. There has been an increase in pre-clinical studies regarding the effects of sirtuins on atherosclerosis and this review aims to highlight the benefits of sirtuins in atherosclerosis. We did an extensive search using the PubMed database with the medical subject headings (MeSH) keywords "sirtuin" and "atherosclerosis." The reviewed literature reported that sirtuins prevent and ameliorate atherosclerosis by halting inflammation, apoptosis, oxidative stress, and regulating low-density lipoprotein (LDL) cholesterol. Sirtuin 1 (SIRT1) and sirtuin 6 (SIRT6) inhibit the RELA component of NF-kB, thus suppressing inflammation, SIRT1 inhibits p53 by deacetylation, and the latter stabilize telomeres thus preventing apoptosis and cell death. Sirtuin 3 (SIRT3) inhibits oxidative stress by driving the production of reduced glutathione. Sirtuin 2 (SIRT2) regulates LDL cholesterol by inhibiting pcsk9, increasing LDL receptors on the cell surface of hepatocytes. A combination of these effects of sirtuins in the endothelial cells suggests sirtuins are anti-atherogenic and could revolutionize the standards for the management of atherosclerosis. This article also emphasizes the need for future research on human cells or subjects rather than animal subjects.

[14] *Yang E, Yoo H, Jang IJ et al.* **Pharmacokinetic and Pharmacodynamic Comparison of Two Formulations of a Fixed-Dose Combination of Gemigliptin/Rosuvastatin 50/20 mg: A Randomized, Open-Label, Single-Dose, Two-Way Crossover Study**. Drug design, development and therapy 2021; 15:651-658.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33628012

ABSTRACT

PURPOSE: A fixed-dose combination (FDC) of gemigliptin/rosuvastatin 50/20 mg as a monolayer tablet has been used to treat patients with both type 2 diabetes mellitus and dyslipidemia. To improve the stability of the FDC, a new FDC formulation as a bilayer tablet was developed. This study aimed to compare the pharmacokinetics (PKs) and pharmacodynamics (PDs) of the FDC of

gemigliptin/rosuvastatin 50/20 mg between the newly developed bilayer tablet and the approved monolayer tablet in healthy subjects. MATERIALS AND METHODS: A randomized, open-label, single-dose, two-treatment, two-way crossover study was conducted. Subjects received a single dose of the FDC of gemigliptin/rosuvastatin 50/20 mg as the bilayer tablet or the monolayer tablet in each period with a 7-day washout. For PK and PD analyses, serial blood samples were collected up to 72 hours after dosing to determine plasma concentrations of gemigliptin, its active metabolite LC15-0636 and rosuvastatin, and plasma dipeptidyl peptidase-4 (DPP-4) activity. PK and PD parameters were calculated using non-compartmental methods and compared between the two formulations. RESULTS: A total of 48 healthy subjects were randomized, and 45 subjects completed the study. The concentration-time profiles of gemigliptin, LC15-0636 and rosuvastatin were comparable between the two formulations. All geometric mean ratios (90% confidence intervals) of the bilayer tablet to the monolayer tablet for maximum plasma concentration and area under concentration-time curve from 0 to last measurable time point of the three compounds fulfilled the bioequivalence criteria of 0.80-1.25. Likewise, area under plasma DPP-4 activity inhibition from baseline-time curve from 0 to last measurable time point and maximum inhibition of plasma DPP-4 activity were similar between the two formulations. CONCLUSION: The FDC of gemigliptin/rosuvastatin 50/20 mg as the bilayer tablet showed equivalent PK and PD properties with the FDC of gemigliptin/rosuvastatin 50/20 mg as the monolayer tablet in healthy subjects. These results suggest that the newly developed bilayer tablet can become an alternative formulation to the commercially available monolayer tablet.

[15] *Lamb YN.* **Inclisiran: First Approval**. Drugs 2021:1-7.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33620677
ABSTRACT
Inclisiran (Leqvio(®); Novartis) is a first-in-class, cholesterol-lowering small interfering RNA (siRNA) conjugated to triantennary N-acetylgalactosamine carbohydrates (GalNAc). Inclisiran received its first approval in December 2020 in the EU for use in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet. It is intended for use in combination with a statin or a statin with other lipid-lowering therapies in patients unable to reach low-density lipoprotein cholesterol goals with the maximum tolerated statin dose. In patients who are statin-intolerant or for whom a statin is contraindicated, inclisiran can be used alone or in combination with other lipid-lowering therapies. Inclisiran is administered as a twice-yearly subcutaneous injection. This article summarizes the milestones in the development of inclisiran leading to this first approval for primary hypercholesterolaemia or mixed dyslipidaemia.

[16] *Robinson GA, Waddington KE, Coelewij L et al.* **Increased apolipoprotein-B:A1 ratio predicts cardiometabolic risk in patients with juvenile onset SLE**. EBioMedicine 2021:103243.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33640328
ABSTRACT
BACKGROUND: Cardiovascular disease is a leading cause of mortality in patients with juvenile-onset systemic lupus erythematosus (JSLE). Traditional factors for cardiovascular risk (CVR) prediction are less robust in younger patients. More reliable CVR biomarkers are needed for JSLE patient stratification and to identify therapeutic approaches to reduce cardiovascular morbidity and mortality in JSLE. METHODS: Serum metabolomic analysis (including >200 lipoprotein measures) was performed on a discovery (n=31, median age 19) and validation (n=31, median age 19) cohort of

JSLE patients. Data was analysed using cluster, receiver operating characteristic analysis and logistic regression. RNA-sequencing assessed gene expression in matched patient samples. FINDINGS: Hierarchical clustering of lipoprotein measures identified and validated two unique JSLE groups. Group-1 had an atherogenic and Group-2 had an atheroprotective lipoprotien profile. Apolipoprotein(Apo)B:ApoA1 distinguished the two groups with high specificity (96.2%) and sensitivity (96.7%). JSLE patients with high ApoB:ApoA1 ratio had increased CD8+ T-cell frequencies and a CD8+ T-cell transcriptomic profile enriched in genes associated with atherogenic processes including interferon signaling. These metabolic and immune signatures overlapped statistically significantly with lipid biomarkers associated with sub-clinical atherosclerosis in adult SLE patients and with genes overexpressed in T-cells from human atherosclerotic plaque respectively. Finally, baseline ApoB:ApoA1 ratio correlated positively with SLE disease activity index (r=0.43, p=0.0009) and negatively with Lupus Low Disease Activity State (r=-0.43, p=0.0009) over 5-year follow-up. INTERPRETATION: Multi-omic analysis identified high ApoB:ApoA1 as a potential biomarker of increased cardiometabolic risk and worse clinical outcomes in JSLE. ApoB:ApoA1 could help identify patients that require increased disease monitoring, lipid modification or lifestyle changes. FUNDING: Lupus UK, The Rosetrees Trust, British Heart Foundation, UCL & Birkbeck MRC Doctoral Training Programme and Versus Arthritis.

[17] *Taha H, Badran HM, Kandil H et al.* **Egyptian practical guidance in lipid management 2020**. The Egyptian heart journal : (EHJ) : official bulletin of the Egyptian Society of Cardiology 2021; 73:17.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33620601

ABSTRACT

BACKGROUND: Numerous epidemiological investigations and randomized clinical studies have determined that dyslipidemia is a major contributor to atherosclerotic cardiovascular disease (ASCVD). Consequently, the management of serum cholesterol and low-density lipoprotein levels has become a central objective in the effort to prevent cardiovascular events. MAIN BODY: Many guidelines were issued by different organizations and societies to define patient risk and establish important recommendations for management strategies. Newer cholesterol-lowering agents (non-statin drugs) are described, and their use is directed primarily to secondary prevention in patients at very high risk of new ASCVD. CONCLUSION: The present guidance summarizes the current methods for risk estimation and outlines the most recent data on lipid management in a simple user-friendly format, to improve physician awareness and help implement guidelines in the daily practice.

[18] *Mitrovic B, Gluvic Z, Macut D et al.* **Effects of Metformin-Single Therapy on the Level of Inflammatory Markers in Serum of Non-Obese T2DM Patients with NAFLD**. Endocrine, metabolic & immune disorders drug targets 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33632113

ABSTRACT

BACKGROUND AND OBJECTIVES: Non-alcoholic fatty liver disease (NAFLD) is associated with inflammation and subsequent increase in cardiovascular risk. Because of its widespread presence and distribution, invasive diagnostic procedures (i.e., liver biopsy) are reserved for a limited number of subjects. With liver ultrasound, Fatty liver index (FLI) and fibrosis-4 (FIB-4) scores non-invasively assess liver steatosis and fibrosis. We aimed to evaluate the changes in inflammatory markers and FLI/FIB-4 scores in non-obese metformin-treated type 2 diabetes patients (T2DM) with NAFLD.

METHODS: All subjects underwent abdominal ultrasound aiming for NAFLD stratification (grade 1 to 3 according to its severity). Metabolic parameters (morning glycaemia, HbA1C, lipids, liver function tests) and serum inflammatory markers (C-reactive protein, ferritin, and nitric oxide), and FLI/FIB-4 are calculated. RESULTS: FLI score and ultrasound NAFLD grades correlated ($p<0.05$). We observed a significant correlation between the levels of ferritin and C-reactive protein (CRP) ($p<0.05$), and the FLI ($p<0.05$). Body weight (BW) ($p<0.05$), waist circumference (WC) ($p<0.05$), the levels of HbA1c ($p<0.05$), transferrin ($p<0.05$), insulin ($p<0.05$), and FLI score ($p<0.05$) significantly differed between groups defined by the severity of NAFLD. CONCLUSION: This pilot study suggests that the serum inflammatory markers at the average normal values point to the sufficiency of metformin-single therapy in inflammation control in non-obese T2DM patients with NAFLD.

[19] *Ota H, Omori H, Kawasaki M et al.* **Clinical impact of PCSK9 inhibitor on stabilization and regression of lipid-rich coronary plaques: a near-infrared spectroscopy study**. European heart journal cardiovascular Imaging 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33637979
ABSTRACT
AIMS: This study aimed to determine the effects of a proprotein convertase subtilisin-kexin type 9 inhibitor (PCSK9i) on coronary plaque volume and lipid components in patients with a history of coronary artery disease (CAD). METHODS AND RESULTS: This prospective, open-label, single-centre study analysed non-culprit coronary segments using near-infrared spectroscopy-intravascular ultrasound (NIRS-IVUS) at baseline and follow-up angiography. Following changes in the lipid-lowering treatment based on the most recent guideline, the enrolled subjects were divided into two groups: treatment with PCSK9i and statins (PCSK9i: 21 patients and 40 segments) and statins only (control: 32 patients and 50 segments). The absolute and percent LDL-C reductions were significantly greater in the PCSK9i group than in the control group (between group difference: 59.3 mg/dL and 46.4%; $P<0.001$ for both). The percent reduction in normalized atheroma volume and absolute reduction in percent atheroma volume (PAV) were also significantly greater in the PCSK9i group ($P<0.001$ for both). Furthermore, the PCSK9i group showed greater regression of maximal lipid core burden index for each of the 4-mm segments (maxLCBI4mm) than the control group (57.0 vs. 25.5; $P=0.010$). A significant linear correlation was found between the percent changes in LDL-C and maxLCBI4mm ($r=0.318$; $P=0.002$), alongside the reduction in PAV ($r=0.386$; $P<0.001$). CONCLUSION: The lipid component of non-culprit coronary plaques was significantly decreased by PCSK9i. The effects of statin combined with PCSK9i might be attributed to the stabilization and regression of residual vulnerable coronary plaques in patients with CAD.

[20] *Mert KU, Başaran Ö, Mert G et al.* **Management of LDL-cholesterol levels in patients with Diabetes Mellitus in Cardiology Practice: Real life evidence of Under-treatment from the EPHESUS registry**. European journal of clinical investigation 2021:e13528.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33630348
ABSTRACT
BACKGROUND AND AIMS: Effective treatment of high low-density lipoprotein cholesterol (LDL-C) levels has been shown to improve cardiovascular outcomes of patients with diabetes mellitus (DM). Herein, we aimed to provide insight to the real-life management of patients with DM in terms of LDL-C goal attainment and adherence to lipid management recommendations. Our objective was also to

reveal the reasons of poor LDL-C goal attainment by assessing the perceptions of both physicians and patients. METHODS: We compared the diabetic and non-diabetic patients from the database of a nation-wide registry conducted in cardiology outpatient clinics with regard to the demographic characteristics, educational status, comorbidities, medications, laboratory parameters, and LDL-C goal attainment. Also, both the patients and attending physicians were surveyed to analyze perceptions and awareness of hypercholesterolemia. RESULTS: Of the 1868 consecutively enrolled patients, 873 (47%) had DM. Proportion of patients on statins was significantly lower in patients with DM (67.8% vs 55.3%; p<0.001). The proportion of patients who attained LDL-C targets were lower among the diabetic patients (17.8% vs 15%; p=0.06). The most common causes of the discontinuation of statin therapy were negative media coverage about statins (32.1%), and recommendations of physicians to stop the lipid lowering therapy (29.6%). Analysis of the physician survey revealed that the physicians could determine the off-target patients accurately (negative predictive value 98.4%) while the positive predictive value (48.8%) was low. The reasons for not attaining the LDL-C goals in diabetic patients were not prescription of statins (38%) and inadequate (e.g., low-dose, non-adherent) statin (28.3%) dosages. CONCLUSIONS: In real-life clinical cardiology practice, diabetic patients are far below the recommended LDL-C treatment goals. High intensity statin treatment in diabetic population is still avoided because of the concerns about polypharmacy and drug interactions. Also, the inertia of physicians and even cardiologists is probably a major cause of refraining of prescription of optimal statin dosages.

[21] *Natorska J, Kopytek M, Undas A*. **Aortic valvular stenosis - novel therapeutic strategies**. European journal of clinical investigation 2021:e13527.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33621361
ABSTRACT
BACKGROUND: Aortic stenosis (AS) prevalence is estimated to reach 4.5 million cases worldwide by the year 2030. AS is a progressive disease without a pharmacological treatment. In the current review we aimed to investigate novel therapeutic approaches for non-surgical AS treatment, at least in patients with mild-to-moderate AS. MATERIALS AND METHODS: The most recent and relevant papers concerned with novel molecular pathways that have potential as therapeutic targets in AS were selected from searches of PubMed and Web of Science up to February 2021. RESULTS: Growing evidence indicates that therapies using proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, simvastatin/ezetimibe combination, cholesteryl ester transfer protein inhibitors or antisense oligonucleotides targeting apolipoprotein(a) reduce the risk of AS progression. It has been shown that enhanced valvular lipid oxidation may drive AS development by leading to the activation of valvular interstitial cells (VICs), the most abundant valvular cells having a major contribution to valve calcification. Since VICs are able to release proinflammatory cytokines, clotting factors, and proteins involved in calcification, strategies targeting these cells activation seem promising as therapeutic interventions. Recently non-vitamin K antagonist oral anticoagulants (NOACs) have been shown to inhibit activation of VICs. CONCLUSION: Several novel molecular pathways of AS development have been identified over the past few years. Therapies using PCSK9 inhibitors, simvastatin/ezetimibe combination, lipoprotein(a)-lowering therapy are highly promising candidates as therapeutics in the prevention of mild AS progression, while preclinical studies show that NOACs may inhibit valvular inflammation and coagulation activation and slower the rate of AS progression.

[22] *Bauer F, Seibert FS, Rohn B et al.* **Estimation of LDL cholesterol in chronic kidney disease**. European journal of preventive cardiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33624033

ABSTRACT

AIMS : Most of the laboratories make use of the Friedewald formula to assess low-density lipoprotein cholesterol (LDL-C). The accuracy of this approach, however, crucially depends on triglyceride concentrations. Since hypertriglyceridaemia is a characteristic trait of the lipid profile in chronic kidney disease (CKD), the present study examines the accuracy of the Friedewald formula in this population. It aims to derive and validate a more accurate equation for CKD. METHODS : Cross-sectional study on two cohorts of subjects (overall n = 3.514) with estimated glomerular filtration rate (eGFR) <60 mL/min comparing directly measured LDL-C (LDL-Cmeas) as assessed by an enzymatic assay (Roche, Switzerland) to concentrations estimated by the Friedewald (LDL-CF) and the Martin's formula (LDL-CM). Accuracy was analysed by Bland-Altman and linear regression analyses. In the first cohort, a novel formula was derived to assess LDL-C in CKD. The formula was validated in Cohort 2. RESULTS : Cohort 1 comprised 1738 subjects, and Cohort 2 comprised 1776 subjects. The mean eGFR was 29.4 ± 14.4 mL/min. In Cohort 1, LDL-CF was highly correlated with LDL-Cmeas (R2 = 0.92) but significantly underestimated LDLmeas by 11 mg/dL. LDL-C = cholesterol - HDL - triglycerides/7.98 was derived as the optimal equation for the calculation of LDL-C in Cohort 1 and was successfully validated in Cohort 2 (bias of 1.6 mg/dL). The novel formula had a higher accuracy than both the Friedewald (bias -12.2 mg/dL) and the Martin's formula (bias -4.8 mg/dL). CONCLUSION : The Friedewald formula yields lower LDL-C concentrations in CKD than direct enzymatic measurements, which may lead to undersupply of this cardiovascular high-risk population in a treat-to-target approach.

[23] *Gaudet D, López-Sendón JL, Averna M et al.* **Safety and efficacy of alirocumab in a real-life setting: the ODYSSEY APPRISE study**. European journal of preventive cardiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33624041

ABSTRACT

AIMS: To obtain safety and efficacy data of alirocumab, a proprotein convertase subtilisin/kexin type 9 inhibitor, in a real-life setting in high cardiovascular (CV) risk patients with heterozygous familial hypercholesterolaemia (HeFH) or very-high low-density lipoprotein cholesterol (LDL-C) levels despite maximally tolerated dose of statin ± other lipid-lowering therapies (MTD ± LLTs). ODYSSEY APPRISE was a prospective, single-arm, Phase 3b open-label (≥12 weeks to ≤ 30 months) European/Canadian study with alirocumab. METHODS AND RESULTS: Patients received alirocumab 75 or 150 mg every 2 weeks, with dose adjustment based on physician's judgment. In total, 994 patients were enrolled and treated. The mean [standard deviation (SD)] duration of alirocumab exposure was 72.4 (42.5) weeks. Patients with HeFH were younger [mean (SD) age of 53.8 (11.6) vs. 61.6 (10.1) years], more likely to be female (41.7% vs. 29.1%) and had higher baseline LDL-C compared with non-familial hypercholesterolaemia (non-FH) patients [mean (SD) of 5.1 (1.7) vs. 4.1 (1.1) mmol/L]. The overall incidence of treatment-emergent adverse events (TEAEs) was 71.6%; common TEAEs included nasopharyngitis (7.8%), myalgia (7.1%), and headache (6.2%). At Week 12, mean (SD) LDL-C was reduced by 54.8 (20.1)% from baseline [2.6 (1.2) mmol/L], maintained for the trial duration. LDL-C was reduced below 1.8 mmol/L and/or by ≥50% reduction from baseline in 69.1% of patients overall, and for 64.7 and 77.4% of the HeFH and non-FH

subgroups, respectively. CONCLUSION: In a real-life setting in patients with hypercholesterolaemia and high CV risk, alirocumab was generally well tolerated and resulted in clinically significant LDL-C reductions.

[24] *Gonzalez-Cantero A, Reddy AS, Dey AK et al.* **Underperformance of clinical risk scores in identifying imaging-based high cardiovascular risk in psoriasis: results from two observational cohorts**. European journal of preventive cardiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33624060
ABSTRACT
AIMS: We aimed to evaluate whether traditional risk scores [short-term, 'psoriasis-modified' (multiplied by 1.5) and lifetime] were able to capture high cardiovascular disease (CVD) risk as defined by the presence of atherosclerotic plaques in coronary, femoral, or carotid arteries in psoriasis. METHODS AND RESULTS: We used two prospectives obseravational cohorts. European cohort: femoral and carotid atherosclerotic plaques were evaluated by ultrasound in 73 psoriasis patients. Lifetime CVD risk (LTCVR) was evaluated with QRISK-LT; short-term CVD risk was evaluated with SCORE and psoriasis-modified SCORE. American cohort: 165 patients underwent coronary computed tomography angiography to assess presence of coronary plaques. LTCVR was evaluated with atherosclerotic cardiovascular disease (ASCVD-LT) lifetime; short-term CVD risk was evaluated with ASCVD and psoriasis-modified ASCVD. European cohort: subclinical atherosclerosis was present in 51% of patients. QRISK-LT identified 64% of patients with atherosclerosis missing a high proportion (35%) with atheroma plaque ($P<0.05$). The percentage of patients with atherosclerosis identified by QRISK-LT was significantly higher than those detected by SCORE (0%) and modified SCORE (10%). American cohort: subclinical atherosclerosis was present in 54% of patients. ASCVD-LT captured 54% of patients with coronary plaques missing a high proportion (46%) with coronary plaque ($P<0.05$). The percentage of patients with atheroma plaques detected with ASCVD and modified ASCVD were only 20% and 45%, respectively. CONCLUSIONS: Application of lifetime, short-term and 'psoriasis-modified' risk scores did not accurately capture psoriasis patients at high CVD risk.

[25] *Khan SU, Khan MU, Virani SS et al.* **Efficacy and safety for the achievement of guideline-recommended lower low-density lipoprotein cholesterol levels: a systematic review and meta-analysis**. European journal of preventive cardiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33624058
ABSTRACT
AIM: The 2018 American Heart Association/American College of Cardiology/Multi-Society Cholesterol Guidelines recommended the addition of non-statins to statin therapy for high-risk secondary prevention patients above a low-density lipoprotein cholesterol (LDL-C) threshold of ≥70 mg/dL (1.8 mmol/L). We compared effectiveness and safety of treatment to achieve lower (<70) vs. higher (≥70 mg/dL) LDL-C among patients receiving intensive lipid-lowering therapy (statins alone or plus ezetimibe or proprotein convertase subtilisin/kexin type 9 inhibitors). METHODS AND RESULTS: Eleven randomized controlled trials (130 070 patients), comparing intensive vs. less-intensive lipid-lowering therapy, with follow-up ≥6 months and sample size ≥1000 patients were selected. Meta-analysis was reported as random effects risk ratios (RRs) [95% confidence intervals] and absolute risk differences (ARDs) as incident cases per 1000 person-years. The median LDL-C levels achieved

in lower LDL-C vs. higher LDL-C groups were 62 and 103 mg/dL, respectively. At median follow-up of 2 years, the lower LDL-C vs. higher LDL-C group was associated with significant reduction in all-cause mortality [ARD -1.56; RR 0.94 (0.89-1.00)], cardiovascular mortality [ARD -1.49; RR 0.90 (0.81-1.00)], and reduced risk of myocardial infarction, cerebrovascular events, revascularization, and major adverse cardiovascular events (MACE). These benefits were achieved without increasing the risk of incident cancer, diabetes mellitus, or haemorrhagic stroke. All-cause mortality benefit in lower LDL-C group was limited to statin therapy and those with higher baseline LDL-C (≥100 mg/dL). However, the RR reduction in ischaemic and safety endpoints was independent of baseline LDL-C or drug therapy. CONCLUSION: This meta-analysis showed that treatment to achieve LDL-C levels below 70 mg/dL using intensive lipid-lowering therapy can safely reduce the risk of mortality and MACE.

[26] *Mahindra MP, Sampurna MTA, Mapindra MP, Sutowo Putri AM*. **Maternal lipid levels in pregnant women without complications in developing risk of large for gestational age newborns: a study of meta-analysis**. F1000Research 2020; 9:1213.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33628433
ABSTRACT
Background: Circulating into foetal circulation across the placental barrier, abnormal maternal serum lipids predispose neonates to metabolic dysfunction and thereafter affect the steroid metabolism and functions of extra-embryonic foetal tissues. Methods: A systematic review was conducted by searching PubMed-MEDLINE and the Cochrane library between January 2010 and January 2020. The included studies were English case control studies that described original data on at least one raw lipid measurement during pregnancy in healthy women who delivered large for gestational age (LGA) newborns and in healthy women with non-LGA newborns. The data extracted from 12 studies were pooled, and the weighted mean difference (WMD) in lipid levels was calculated using random effects models. A meta-analysis was performed to identify sources of heterogeneity and to describe the significant value of the collected studies. Results: Of 649 published articles identified, a total of 12 met the inclusion criteria . Compared with women who had non-LGA newborns, those who had LGA newborns had significantly higher triglyceride (TG) levels (WMD = 0.28, 95% CI -0.02 to 0.54) and lower high density lipoprotein cholestrol (HDL-C) levels (WMD = 0.08, 95% CI -0.13 to -0.03), but not have significantly lower high-density lipoprotein cholesterol (LDL-C) levels. Moreover, the levels of total cholesterol, low-density lipoprotein cholesterol, and very low density lipoprotein cholesterol (VLDL-C) were inconsistent between both groups. Conclusions: High levels of TG and low levels of HDL-C could cause births of LGA newborns whereas maternal serum of TC, LDL-C and VLDL-C cannot be used as predictor of LGA.

[27] *Mousapour P, Barzin M, Valizadeh M et al.* **Comparison of the Modification of Diet in Renal Disease Study and Chronic Kidney Disease Epidemiology Collaboration Equations for Detection of Cardiovascular Risk: Tehran Lipid and Glucose Study**. International journal of endocrinology and metabolism 2020; 18:e101977.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33613676
ABSTRACT
OBJECTIVES: The study aimed to compare the Modification of Diet in Renal Disease Study (MDRD) and the Epidemiology Collaboration (CKD-EPI) equations for the detection of cardiovascular risk.

METHODS: Data of 9,970 Tehranian participants aged ≥ 20 years were analyzed. The prevalence of cardiovascular disease (CVD), its risk factors, and 10-year atherosclerotic cardiovascular disease (ASCVD) risk were compared across the categories of glomerular filtration rate based on the MDRD and CKD-EPI equations. Chronic kidney disease (CKD) was defined as the estimated Glomerular Filtration Rate (eGFR) < 60 mL/min/1.73 m(2) according to each equation. RESULTS: The prevalence of CKD weighted to the 2016 Tehranian urban population was 11.0% (95% confidence interval: 10.3 - 11.6) and 9.7% (9.1 - 10.2) according to the MDRD and CKD-EPI equations, respectively. Besides, 8.3% and 1.5% of the participants with CKD(MDRD) and non-CKD(MDRD) were reclassified to non-CKD(CKD-EPI) and CKD(CKD-EPI) categories, respectively. Participants with CKD(CKD-EPI) but without CKD(MDRD) were more likely to be male and older, and more frequently had diabetes, hypertension, dyslipidemia, and CVD, when compared to those without CKD according to both equations; they were also more likely to be male, older, and smokers, and had less dyslipidemia and more CVD, when compared to those with CKD by using both equations. In multivariate logistic regression analysis, compared to CKD(MDRD), the odds of CKD(CKD-EPI) were significantly higher for older age and lower for the female gender. CONCLUSIONS: Compared to MDRD, the CKD-EPI equation provides more appropriate detection of cardiovascular risk, which is caused by the reclassification of older individuals and fewer females into lower eGFR categories.

[28] *Catov JM, McNeil RB, Marsh DJ et al.* **Early Pregnancy Atherogenic Profile in a First Pregnancy and Hypertension Risk 2 to 7 Years After Delivery**. Journal of the American Heart Association 2021; 10:e017216.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33619977

ABSTRACT

Background Cardiovascular risk in young adulthood is an important determinant of lifetime cardiovascular disease risk. Women with adverse pregnancy outcomes (APOs) have increased cardiovascular risk, but the relationship of other factors is unknown. Methods and Results Among 4471 primiparous women, we related first-trimester atherogenic markers to risk of APO (hypertensive disorders of pregnancy, preterm birth, small for gestational age), gestational diabetes mellitus (GDM) and hypertension (130/80 mm Hg or antihypertensive use) 2 to 7 years after delivery. Women with an APO/GDM (n=1102) had more atherogenic characteristics (obesity [34.2 versus 19.5%], higher blood pressure [systolic blood pressure 112.2 versus 108.4, diastolic blood pressure 69.2 versus 66.6 mm Hg], glucose [5.0 versus 4.8 mmol/L], insulin [77.6 versus 60.1 pmol/L], triglycerides [1.4 versus 1.3 mmol/L], and high-sensitivity C-reactive protein [5.6 versus 4.0 nmol/L], and lower high-density lipoprotein cholesterol [1.8 versus 1.9 mmol/L]; P<0.05) than women without an APO/GDM. They were also more likely to develop hypertension after delivery (32.8% versus 18.1%, P<0.05). Accounting for confounders and factors routinely assessed antepartum, higher glucose (relative risk [RR] 1.03 [95% CI, 1.00-1.06] per 0.6 mmol/L), high-sensitivity C-reactive protein (RR, 1.06 [95% CI, 1.02-1.11] per 2-fold higher), and triglycerides (RR, 1.27 [95% CI, 1.14-1.41] per 2-fold higher) were associated with later hypertension. Higher physical activity was protective (RR, 0.93 [95% CI, 0.87-0.99] per 3 h/week). When evaluated as latent profiles, the nonobese group with higher lipids, high-sensitivity C-reactive protein, and insulin values (6.9% of the cohort) had increased risk of an APO/GDM and later hypertension. Among these factors, 7% to 15% of excess RR was related to APO/GDM. Conclusions Individual and combined first-trimester atherogenic characteristics are

associated with APO/GDM occurrence and hypertension 2 to 7 years later. Registration URL: https://www.clinicaltrials.gov; Unique identifier: NCT02231398.

[29] *Garcés MF, Guarin Y, Carrero Y et al.* **Fat Intolerance in Apparently Healthy Individuals with Normal Fasting Lipoproteins Is Associated with Markers of Cardiovascular Risk**. J Appl Lab Med 2016; 1:250-259.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33626837
ABSTRACT
BACKGROUND: Postprandial increase of triglyceride-rich lipoproteins augments the risk of atherosclerotic cardiovascular disease and all-cause mortality. We explored the hypothesis that a simplified oral fat tolerance test can uncover differences in postprandial triglyceride response associated with potentially atherogenic lipoprotein characteristics, even in a cohort of apparently healthy 31-year-old [mean (SD), 31 (11)] nonobese individuals with normal fasting lipids and lipoproteins. METHODS: We used a fat tolerance test in 96 females and 62 males with blood sampled at 0, 2, and 4 h after a breakfast containing 26.3 g of fats. The postprandial triglyceride response was used to classify the individuals in apparently fat-tolerant and apparently fat-intolerant participants. RESULTS: The intolerant individuals were found to have at 0 h significantly higher body mass index, plasma triglycerides, remnant cholesterol, VLDL cholesterol, and LDL cholesterol and lower apolipoprotein (apo) AI and HDL cholesterol than the tolerant individuals. More than 70% of the variability (r2) of the postprandial response in tolerant and intolerant individuals measured as area under the curve or, at a single point at 4 h after the oral fat load, was linearly correlated with 0-h triglycerides ($P < 0001$). Fasting lipoprotein parameters, proposed to be markers of cardiovascular risk, as the ratios apo B/apo AI, total cholesterol/HDL cholesterol, and triglycerides/HDL cholesterol, were increased in the intolerant individuals. CONCLUSIONS: A simplified oral fat tolerance test, even when used in an apparently healthy, nonobese, normolipidemic cohort, detected that an increased postprandial triglycerides response was associated with augmented lipoprotein markers of increased cardiovascular risk.

[30] *Nakamura M, Ako J, Arai H et al.* **Lipid Management and 2-Year Clinical Outcomes in Japanese Patients with Acute Coronary Syndrome: EXPLORE-J**. Journal of atherosclerosis and thrombosis 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33612707
ABSTRACT
AIM: The prevalence of atherosclerotic cardiovascular (CV) disease has risen in Japan due to increasing metabolic risk factors, including dyslipidemia. A positive linear correlation between low-density lipoprotein cholesterol (LDL-C) levels, incidence of CV events, and preventive effects of lipid-lowering therapy (LLT) is well established; however, data in Japan are limited. This analysis evaluated current lipid management practices and risk of recurrent CV events in Japanese post-acute coronary syndrome (ACS) patients. METHODS: EXPLORE-J is a multicenter, 2-year observational study of hospitalized ACS patients in Japan. RESULTS: At 2-year follow-up (n=1944, mean age 66 years, 80.3% male), the cumulative incidence of major adverse cardiovascular events (MACE; death associated with myocardial infarction/cerebrovascular accident [CVA] and other CV death, non-fatal ACS, and non-fatal CVA requiring hospitalization during the observation period) was 6.2%; respective incidences of CV death, non-fatal ACS, and CVA were 0.7%, 4.5%, and 1.7%. Statin, intensive statin,

and ezetimibe were prescribed for 93.6%, 8.2%, and 3.9% at visit (V)1 (Day[D]1＋14), and 92.3%, 10.5%, and 11.6% of patients at V5 (D730±30 days), respectively. Mean LDL-C was reduced from first post-ACS measurement (121.3 mg/dL) to V5 (79.8 mg/dL). A limited number of patients achieved LDL-C ＜70 mg/dL from V1-V5 (14.4%-34.6%); those with a greater LDL-C reduction by V1 had a lower probability of MACE, indicating the benefits of early LDL-C reduction post ACS. CONCLUSIONS: Guideline-recommended LDL-C target achievement post ACS in Japan is suboptimal, suggesting the need for LLT intensification. Additional analyses by risk stratification of the study population and the benefits of lipid management are planned.

[31] *Pedersen E, Truong KNL, Garcia BH et al.* **Self-reported medication use among coronary heart disease patients showed high validity compared with dispensing data**. J Clin Epidemiol 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33640414
ABSTRACT
OBJECTIVE: To validate self-reported use of medications for secondary prevention of coronary heart disease (CHD) in a population-based health study by comparing self-report with pharmacy dispensing data, and explore different methods for defining medication use in prescription databases. STUDY DESIGN AND SETTING: Self-reported medication use among participants with CHD (n=1483) from the seventh wave of the Tromsø Study was linked with the Norwegian Prescription Database (NorPD). Cohen´s kappa, sensitivity, specificity, and positive and negative predictive values were calculated, using NorPD as the reference standard. Medication use in NorPD was defined in three ways; fixed-time window of 180 days, and legend-time method assuming a daily dose of one dosage unit or one defined daily dose (DDD). RESULTS: Kappa-values for antihypertensive drugs, lipid-lowering drugs and acetylsalicylic acid all showed substantial agreement (kappa ≥0.61). Validity varied depending on the method used for defining medication use in NorPD. Applying a fixed-time window gave higher agreement, positive predictive values and specificity compared with the legend-time methods. CONCLUSION: Self-reported use of medication for secondary prevention of CHD shows high validity when compared with pharmacy dispensing data. For CHD medications, fixed-time window appears to be the most appropriate method for defining medication use in prescription databases.

[32] *Wang M, Li M, Xie Y.* **The association between statins exposure and peripheral neuropathy risk: A meta-analysis**. Journal of clinical pharmacy and therapeutics 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33629752
ABSTRACT
WHAT IS KNOWN AND OBJECTIVE: Statins are widely used lipid-lowering drugs and play an important role in the treatment of many cardiovascular diseases. With the increase in the scope of use and the number of users, peripheral neuropathy caused by statins has been frequently reported. There are no randomized controlled trials comparing the relationship between statins and the risk of peripheral neuropathy. Therefore, we systematically reviewed and meta-analysed observational studies evaluating the impact of statins on the risk of peripheral neuropathy. METHODS: PubMed, Embase, the Cochrane Library databases and Web of Science were used to search the effects of statins on polyneuropathy from inception to 3 December 2020. We included studies that met the

following criteria: (i) A randomized controlled trial, prospective or retrospective cohort study examining the relationship between statins and peripheral neuropathy (PN). Exclusion criteria included the following: Reviews and research related to other diseases or subjects; and studies without data on the prevalence of PN were excluded. Newcastle-Ottawa scale (NOS) was used for quality assessment of included studies. Meta-analysis was used to estimate the risk of disease. We conducted a subgroup analysis of duration of follow-up, adjusted (adjusted RR vs. unadjusted RR), sample size, study design and region. RESULTS AND DISCUSSION: A total of 9 independent studies assessing 150 556 patients were included in this analysis. In this meta-analysis, we found that there was a nonsignificant increase of PN with statins exposure (RR 1.26, 95% CI (0.92-1.74)). Our results revealed that there was no significant association between statins exposure and peripheral neuropathy risk. WHAT IS NEW AND CONCLUSION: Statins exposure does not influence the risk of developing peripheral neuropathy. The quality of the evidence included in this study is low, but it can provide useful information for clinicians.

[33] *Dias GD, Cartolano FC, Freitas MCP et al.* **Adiponectin predicts the antioxidant capacity and size of high-density lipoprotein (HDL) in individuals with diabetes mellitus**. Journal of diabetes and its complications 2021:107856.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33627254
ABSTRACT
AIMS: The relationship between adiponectin and type 2 diabetes mellitus (T2DM) is established; however the evidence on its role in high-density lipoprotein (HDL) functionality is still scant. The aim of this study was to assess the association of adiponectin with HDL functionality especially on the antioxidant capacity and HDL subfractions in individuals with T2DM. METHODS: This case-control study enrolled 356 individuals who were divided into two groups: diabetics [T2DM (n = 188)] and non-diabetic [nT2DM (n = 168)]. The association of adiponectin level on HDL functionality parameters was done in function of the cut-off point for adiponectin [percentile p < 75 = 12.9 μg/mL versus p ≥ 75 = 12.9 μg/mL] and multiple adjustments applied in the logistic regression models. RESULTS: Body mass index (BMI), waist circumference (WC) and body fat mass (FM) were higher in T2DM. The larger HDL particles (HDL(LARGE)) were lower in T2DM group in comparison with nT2DM (28.20% versus 30.40%; p = 0.016). Individuals with T2DM and simultaneous highest adiponectin (p ≥ 75) had 2.25 OR (95% CI = 1.03-4.91) and 5.14 OR (95% CI = 2.37-11.15) to present higher HDL-C and HDL(LARGE) concentrations. After adjustment for multiple confounders, high level of adiponectin was independently related with improvement of the HDL antioxidant capacity (OR = 2.78; 95% CI = 1.16-6.67). CONCLUSIONS: High adiponectin level associates with a lesser negative impact of T2DM on HDL functionality by increase in APO AI, particles size, and cholesterol content. On the same token, higher adiponectin was associated with greater odds to have high antioxidant capacity.

[34] *Zhang W, Yang J, Liu J et al.* **Red yeast rice prevents chronic alcohol-induced liver disease by attenuating oxidative stress and inflammatory response in mice**. J Food Biochem 2021:e13672.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33624852
ABSTRACT

Alcoholic liver disease (ALD) is characterized by dyslipidemia, hepatic steatosis, steatohepatitis, edema, necrosis, etc. Studies have reported that some dietary nutrition factors have beneficial effects in improving ALD. Red yeast rice (RYR), a traditional herbal supplement, has been confirmed to lower cholesterol mainly due to its component monacolin K. However, the effect of RYR on ALD has not been investigated. In this study, mice were supplemented with a daily oral gavage of 4 g/kg 50% ethanol for 8 weeks to induce a chronic ALD. RYR (150 mg kg(-1) day(-1)) was supplied to ALD mice in treatment group. The results showed that RYR supplementation significantly attenuated hyperlipidemia, elevated circulating inflammatory cytokines, hepatic structural damage, and oxidative stress in mice supplemented with alcohol with no effects on body weight. Moreover, RYR significantly suppressed alcohol-induced hepatic NF-κB activation and apoptosis. Our results suggest that RYR is capable of preventing ALD mainly by attenuating hepatic oxidative stress and inflammatory response. PRACTICAL APPLICATIONS: RYR was known for cholesterol-lowering effect through its main component monacolin K. The current study revealed that RYR was capable of ameliorating ALD, which is characterized by profound dyslipidemia, hepatic steatosis, steatohepatitis, edema, etc. Our results indicated that the protective effect of RYR on ALD is largely achieved by regulating lipid metabolism, and closely related to the anti-inflammatory and antioxidant effects of RYR. This study provides research foundation for the development of RYR-related food or pharmaceutical products, especially targeting for ALD.

[35] *Yeang C, Witztum JL, Tsimikas S*. **Novel method for quantification of lipoprotein(a)-cholesterol: Implications for improving accuracy of LDL-C measurements**. Journal of lipid research 2021:100053.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33636163
ABSTRACT
Current methods for determining "LDL-C" in clinical practice measure the cholesterol content of both LDL and lipoprotein(a) [Lp(a)-C]. We developed a high-throughput, sensitive and rapid method to quantitate Lp(a)-C and improve the accuracy of "LDL-C" by subtracting for Lp(a)-C (LDL-C(corr)). Lp(a)-C is determined following isolation of the Lp(a) lipoprotein on magnetic beads linked to monoclonal antibody LPA4 recognizing apolipoprotein(a). This Lp(a)-C assay does not detect cholesterol in plasma samples lacking Lp(a) and is linear up to 747 nM Lp(a). To validate this method clinically over a wide range of Lp(a) [9.0-822.8 nM], Lp(a)-C and LDL-C(corr) were determined in 21 participants receiving an Lp(a)-specific lowering ASO and in 8 participants receiving placebo at baseline, at 13-weeks during peak drug effect and off drug. In the groups combined, Lp(a)-C ranged from 0.6-35.0 mg/dL and correlated with Lp(a) molar concentration ($r=0.76$, $p<0.001$). However, the percent Lp(a)-C relative to Lp(a) mass varied from 5.8-57.3%. Baseline LDL-C(corr) was lower than "LDL-C" (mean [SD]) 102.2 (31.8) versus 119.2 (32.4) mg/dL, $p < 0.001$) and did not correlate with Lp(a)-C. It was demonstrated that 3 commercially-available "direct LDL-C" assays also include measures of Lp(a)-C. In conclusion, we have developed a novel and sensitive method to quantitate Lp(a)-C that provides insights into the Lp(a) mass/cholesterol relationship and may be used to more accurately report LDL-C and re-assess its role in clinical medicine.

[36] *Zhang L, Zhu L, Lu M et al.* **Comparison of Carotid Plaque Characteristics Between Men and Women Using Magnetic Resonance Vessel Wall Imaging: A Chinese Atherosclerosis Risk Evaluation Study**. Journal of magnetic resonance imaging : JMRI 2021.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33638575

ABSTRACT

BACKGROUND: Carotid vulnerable plaque is a major cause of stroke and differs between men and women. Few studies have investigated the differences in carotid plaque features between sexes in a Chinese population. PURPOSE: To compare carotid atherosclerotic plaque features between men and women in a Chinese population using magnetic resonance imaging. STUDY TYPE: Cross-sectional. SUBJECTS: A total of 567 patients (mean age: 61.5 ± 10.1 years; 404 men) who had recent stroke or transient ischemia attack and atherosclerotic plaque in at least one carotid artery. FIELD STRENGTH: A 3.0 T. SEQUENCE: T1- and T2-weighted turbo spin echo, three-dimensional time-of-flight (TOF) fast field echo and magnetization-prepared rapid acquisition gradient echo sequences. ASSESSMENT: Plaque characteristics including lumen area (LA), wall area (WA), total vessel area (TVA), mean wall thickness (MWT), and mean normalized wall index (NWI); presence of calcification, lipid-rich necrotic core (LRNC), intraplaque hemorrhage (IPH), and fibrous cap rupture (FCR); and percent composition area (%area) were evaluated and compared between men and women. STATISTICAL TESTS: Independent-sample t test, Mann-Whitney U test, chi-square test, and multiple linear and logistic regressions. RESULTS: In symptomatic arteries, men had significantly greater LA (46.2 ± 15.6 mm(2) vs. 40.7 ± 12.9 mm(2) , P < 0.05), WA (33.9 ± 11.5 mm(2) vs. 26.3 ± 7.5 mm(2) , P < 0.05), and TVA (80.1 ± 20.4 mm(2) vs. 67.0 ± 18.0 mm(2) , P < 0.05); higher MWT (1.2 ± 0.4 mm vs. 1.0 ± 0.2 mm, P < 0.05); and higher prevalence of LRNC (72.3% vs. 46.0%, P < 0.05) and IPH (18.6% vs. 4.9%, P < 0.05) compared with women. In asymptomatic arteries, men had significantly greater LA (48.3 ± 16.9 mm(2) vs. 42.1 ± 12.6 mm(2) , P < 0.05), WA (32.9 ± 11.0 mm(2) vs. 25.8 ± 6.1 mm(2) , P < 0.05), and TVA (81.2 ± 22.1 mm(2) vs. 67.9 ± 16.5 mm(2) , P < 0.05); higher MWT (1.2 ± 0.3 mm vs. 1.0 ± 0.2 mm, P < 0.05); higher prevalence of LRNC (67.8% vs. 42.9%, P < 0.05), IPH (14.9% vs. 1.2%, P < 0.05), and FCR (6.4% vs. 1.2%, P < 0.05); and higher %LRNC area (24.8 ± 17.2% vs. 17.8 ± 14.1%, P < 0.05) compared with women. DATA CONCLUSION: Men have similar plaque burden but more vulnerable atherosclerotic plaques compared with women in both symptomatic and asymptomatic carotid arteries in a Chinese population. EVIDENCE LEVEL: 4 TECHNICAL EFFICACY: Stage 3.

[37] *Burnap SA, Mayr M.* **Lipoprotein compartmentalisation as a regulator of PCSK9 activity**. Journal of molecular and cellular cardiology 2021; 155:21-24.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33617869

ABSTRACT

[38] *Fiz F, Piccardo A, Morbelli S et al.* **Longitudinal analysis of atherosclerotic plaques evolution: an (18)F-NaF PET/CT study**. Journal of nuclear cardiology : official publication of the American Society of Nuclear Cardiology 2021.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33630243

ABSTRACT

PURPOSE: (18)F-NaF-PET/CT can detect mineral metabolism within atherosclerotic plaques. To ascertain whether their (18)F-NaF uptake purports progression, this index was compared with subsequent morphologic evolution. METHODS: 71 patients underwent two consecutive (18)F-NaF-PET/CTs (PET1/PET2). In PET1, non-calcified (18)F-NaF hot spots were identified in the abdominal aorta. Their mean/max HU was compared with those of a non-calcified control region (CR) and with

corresponding areas in PET2. A target-to-background ratio (TBR), mean density (HU), and calcium score (CS) were calculated on calcified atherosclerotic plaques in PET1 and compared with those in PET2. A VOI including the entire abdominal aorta was drawn; mean TBR and total CS were calculated on PET1 and compared with those PET2. RESULTS: Hot spots in PET1 (N = 179) had a greater HU than CR (48 ± 8 vs 37 ± 9, P < .01). Mean hot spots HU increased to 59 ± 12 in PET2 (P < .001). New calcifications appeared at the hot spots site in 73 cases (41%). Baseline atherosclerotic plaque's (N = 375) TBR was proportional to percent HU and CS increase (P < .01 for both). Aortic CS increased (P < .001); the whole-aorta TBR in PET1 correlated with the CS increase between the baseline and the second PET/CT (R = .63, P < .01). CONCLUSIONS: (18)F-NaF-PET/CT depicts the early stages of plaques development and tracks their evolution over time.

[39] *Ahmad A, Isherwood C, Umpleby M, Griffin B*. **Effects of High and Low Sugar Diets on Cardiovascular Disease Risk Factors**. Journal of nutritional science and vitaminology 2020; 66:S18-s24.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33612591
ABSTRACT
It has been proposed that a high sugar intake was associated with cardiovascular disease (CVD) risk and metabolic syndrome depending on the amount of carbohydrate (CHO), other nutrients in foods, and underlying metabolic disturbances. This study aimed to investigate the effects of high (HS) and low sugar (LS) diets on metabolic profiles in 25 middle-aged men at increased CVD risk in a 12-week randomised cross-over intervention study. An isocaloric dietary exchanged model consisted of HS (24% energy from sugar) and LS (6% energy from sugar) with comparable total CHO, fat and fibre composition in normal foods was used. Anthropometric, blood pressure and plasma lipid profile were measured pre- and post-intervention. Body weight, waist circumference and fat mass increased and decreased significantly after HS (by 0.7±0.3 kg, 1.4±1.0 cm and 0.5±0.3 kg) and LS (by 2.1±0.5 kg, 2.0±0.8 cm and 1.4±0.3 kg) ($p<0.05$), respectively. Plasma TG increased significantly after HS by 0.26±0.07 mmol/L and decreased after LS by 0.35±0.16 mmol/L. Plasma HDL decreased by 0.11±0.03 mmol/L ($p<0.05$) after HS, whilst, plasma TC and LDL decreased significantly by 10% after LS. There was no significant change in other parameters after either diet. This study confirmed that a diet with a greater proportion of sugar increased CVD risk via negative changes in metabolic profiles including body weight, waist circumference and lipid parameters, whereas LS produced the positive effects. A restriction of sugar intake to lower than 10% energy intake is vital to reduce CVD risk.

[40] *Chen K, Guo J, Zhang T et al.* **The Role of Dyslipidemia in Colitis-Associated Colorectal Cancer**. J Oncol 2021; 2021:6640384.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33628242
ABSTRACT
Dyslipidemia, characterized by metabolic abnormalities, has become an important participant in colorectal cancer (CRC). Dyslipidemia aggravates intestinal inflammation, destroys the protective mucous layer, and disrupts the balance between injury and recovery. On the other hand, antioxidants induced by oxidative stress enhance glycolysis to maintain the acquisition of ATP allowing epithelial cells with damaged genomes to survive. In the repetitive phase of colitis, survival factors enable these epithelial cells to continuously proliferate. The main purpose is to restore and rebuild damaged mucosa, mainly aiming to recover mucosal damage and reconstruct mucosa, but it is also implicated

in the occurrence and malignancy of CRC. The metabolic reprogramming of aerobic glycolysis and lipid synthesis enables these transformed epithelial cells to convert raw carbohydrate and amino acid substrates, thereby synthesizing protein and phospholipid biomass. Stearoyl-CoA desaturase, responsible for the fatty acid desaturation, improves the fluidity and permeability of cell membranes, which is one of the key factors affecting metabolic rate. In response to available fat, tumor cells reprogram their metabolism to better plunder energy-rich lipids and rapidly scavenge these lipids through continuous proliferation. However, lipid metabolic disorders inhibit the function of immune-infiltrating cells in the tumor microenvironment through the cross-talk between tumor cells and immunosuppressive stromal cells, thereby providing opportunities for tumor progress. Nonsteroidal anti-inflammatory drugs and lipid-lowering drugs can decrease the formation of aberrant crypt foci, lower the burden of the adenomatous polyp, and reduce the incidence of CRC. This review provides a comprehensive understanding of dyslipidemia on tumorigenesis and tumor progression and a development prospect of lipid disorders on tumor immunity.

[41] *Rao AK, Del Carpio-Cano F, Janapati S et al.* **Effects of Simvastatin on Tissue Factor Pathway of Blood Coagulation in STATCOPE (Simvastatin in the Prevention of COPD Exacerbations) Trial**. Journal of thrombosis and haemostasis : JTH 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33638931
ABSTRACT
BACKGROUND: Statins are widely used to lower lipids and reduce cardiovascular events. In vitro studies and small studies in patients with hyperlipidemias show statins inhibit tissue factor (TF) and blood coagulation mechanisms. We assessed the effects of simvastatin on TF and coagulation biomarkers in patients entered in STATCOPE, a multicenter, randomized, placebo-controlled trial of simvastatin (40 mg daily) versus placebo on exacerbation rates in patients with chronic obstructive pulmonary disease (COPD). METHODS: In 227 patients (114 simvastatin; 113 placebo; mean (±SEM) age 62 ± 0.53 years, 44.5 % women) we measured (baseline; 6 and 12 months): whole blood membrane TF-procoagulant activity (TF-PCA) and plasma factors VIIa, VII, VIII, fibrinogen, TF antigen, tissue factor pathway inhibitor (TFPI), thrombin-antithrombin complexes (TAT) and D-dimer. We excluded patients with diabetes, cardiovascular disease and those taking or requiring a statin. RESULTS: In the statin group, there was a small increase in TF-PCA (from 25.18±1.08 to 30.36±1.10 U/ml; p=0.03) over 12 months; factors VIIa and VIII, fibrinogen, TAT and D-dimer did not change. Plasma TFPI (from 52.4±1.75 to 44.7±1.78 ng/mL; p< 0.0001) and FVIIC (1.23±0.04 to 1.15±0.03 U/mL; p=0.03) decreased and correlated with total cholesterol levels. No changes in biomarkers were observed with placebo. CONCLUSIONS: In contrast to previous studies on statins, in COPD patients without diabetes, cardiovascular disease or requiring a statin treatment, simvastatin (40 mg per day) did not decrease TF or factors VIIa and VIII, fibrinogen, TAT or D-dimer. The decreases in TFPI and factor VII reflect the decrease in serum lipids.

[42] *Lim HY, Lui B, Tacey M et al.* **Global coagulation assays in healthy controls: are there compensatory mechanisms within the coagulation system?** Journal of thrombosis and thrombolysis 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33625645
ABSTRACT

Global coagulation assays (GCAs) may provide a more comprehensive individual hemostatic profiling. We aim to evaluate GCAs (thromboelastography, thrombin generation) in healthy controls, and correlate results with age, gender, lipid status, tissue factor pathway inhibitor (TFPI) and P-selectin. Blood samples were collected from healthy controls (>18 years of age) not taking anticoagulation or antiplatelet agents and without known cardiovascular disease. Thromboelastography (TEG) was performed on citrated whole blood while calibrated automated thrombogram (CAT), P-selectin (endothelial marker) and TFPI (principle inhibitor of tissue factor-initiated coagulation) were performed on platelet-poor plasma. 153 healthy controls (mean age 42 years, 98 females (64%)) were recruited. Female controls demonstrated more hypercoagulable TEG and CAT parameters while those over 50 years of age demonstrated more hypercoagulable TEG parameters despite comparable thrombin generation. Paradoxically, individuals with "flattened" thrombin curves (lower velocity index (rate of thrombin generation) despite preserved endogenous thrombin potential (amount of thrombin)) were more likely to be male (49% vs 20%, p=0.003) with increased low-density lipoprotein cholesterol (3.3 vs 2.6 mmol/L, p=0.003), P-selectin (54.2 vs 47.3 ng/mL, p=0.038) and TFPI (18.7 vs 8.6 ng/ml, p=0.001). In addition to reduced velocity index and thrombin peak, controls in the highest TFPI tertile also demonstrated a poorer lipid profile. GCAs can detect subtle changes of the hemostatic profile. Interestingly, reduced thrombin generation was paradoxically associated with increased cardiovascular risk factors, possibly attributable to increased TFPI. This finding may suggest compensation by the coagulation system in response to endothelial activation and represent a biomarker for early cardiovascular disease. A larger prospective study evaluating these assays in the cardiovascular disease population is ongoing.

[43] *Kongmalai T, Chuanchaiyakul N, Sripatumtong C et al.* **The effect of temperature on the stability of PCSK-9 monoclonal antibody: an experimental study**. Lipids in health and disease 2021; 20:21.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33632254
ABSTRACT
BACKGROUND: PCSK9 monoclonal antibody lowers plasma PCSK9 and LDL-cholesterol levels. The manufacturers recommend drug storage at 2-8 °C, and not above 25 °C. This study aimed to investigate drug stability at various temperatures that this drug could be exposed to during medication handling and transportation in tropical countries. METHODS: Alirocumab and evolocumab were tested in 3 study conditions: room temperature (RT), cooler device with cold pack, and freeze-thaw for 9 and 18 h. Heated drugs were used as negative control. Free plasma PCSK9 levels from 9 hyperlipidemia subjects were measured with ELISA. RESULTS: Average subject age was 49.2 ± 18.4 years. Percent PCSK9 inhibition significantly declined in heated drugs compared to baseline. Average RT during the study period was 30.4 ±2.6 °C. Change in percent PCSK9 inhibition of PCSK9 mAb at RT from baseline was - 5.8 ± 4.4% (P = 0.005) and - 11.0 ± 8.9% (P = 0.006) for alirocumab at 9 h and 18 h, and - 9.7 ± 11.8% (P = 0.04) and - 15.1 ± 14.3% (P = 0.01) for evolocumab at 9 and 18 h, respectively. In contrast, there were no significant changes in percent PCSK9 inhibition from baseline when PCSK9 mAb was stored in a cooler. In freeze-thaw condition, changes in percent PCSK9 inhibition from baseline to 9 and 18 h were - 5.2 ± 2.9% (P = 0.001) and - 2.6 ± 4.9% (P = 0.16) for alirocumab, and - 1.8 ± 4.2% (P = 0.24) and 0.4 ± 6.1% (P = 0.83) for evolocumab. CONCLUSION: Proper drug storage according to manufacturer's recommendation is essential. Drug storage at RT in

tropical climate for longer than 9 h significantly decreased drug efficacy; however, storage in a cooler device with cold pack for up to 18 h is safe.

[44] *Xie B, He J, Liu Y et al.* **A meta-analysis of HDL cholesterol efflux capacity and concentration in patients with rheumatoid arthritis**. Lipids in health and disease 2021; 20:18.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33612101

ABSTRACT

BACKGROUND: Poor cholesterol efflux capacity (CEC) has been proposed to be an independent risk factor for cardiovascular diseases. However, current evidence is inconsistent, especially in rheumatoid arthritis (RA) patients. This meta-analysis aims to identify whether CEC is impaired or altered by drug therapy in RA. METHODS: The PubMed/MEDLINE, Embase, Cochrane Library and ClinicalTrials.gov databases were browsed to identify studies on CEC in RA patients. The searches mainly focused on studies in human subjects that were published before November 14, 2020, without any language restrictions. The effect size was pooled by the standardized mean differences and mean differences (SMD & MD) as well as the corresponding 95% confidence intervals (CIs) in a random or fixed effect model. Heterogeneity across the studies was tested using Cochran's Q test and I(2) statistic. Newcastle-Ottawa Scale and the Downs and Black scale (D&B) were applied to evaluate the quality of included studies. The GRADE-system with its 4-grade evidence scale was used to assess the quality of evidence. RESULTS: A total of 11 eligible articles, including 6 observational and 5 interventional studies, were retrieved. The pooled results showed that in patients with RA, CEC was not significantly different than in healthy controls (SMD: -0.34, 95% CI: -0.83 to 0.14), whereas the plasma HDL-C levels was significantly lower (MD: -3.91, 95% CI: -7.15 to -0.68). Furthermore, in the before-after studies, the CEC of RA patients (SMD: 0.20, 95% CI: 0.02 to 0.37) increased, but the plasma HDL-C levels (MD: 3.63, 95% CI: -0.13 to 7.39) remained at a comparable quantity after anti-rheumatic treatment comparing with the baseline. In addition, the funnel plot of included studies displayed a lightly asymmetry, while Egger's and Begg's test did not suggest the existence of publication bias. The quality of evidence was rated according to GRADE as moderate to very low. CONCLUSION: The current meta-analysis demonstrated that HDL-mediated CEC can be improved by the early control of inflammation and anti-rheumatic treatment in RA patients, which is independent of the plasma HDL-C levels. However, the results should be interpreted with caution because of low-quality and limited quantity of evidence. Future randomized controlled trials are needed to determine whether therapeutic strategies to enhance CEC in RA patients have beneficial effects for preventing CVD.

[45] *Guo Y, Zou G, Qi K et al.* **Simvastatin impairs hippocampal synaptic plasticity and cognitive function in mice**. Mol Brain 2021; 14:41.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33627175

ABSTRACT

Lipophilic statins which are blood brain barrier (BBB) permeable are speculated to affect the cholesterol synthesis and neural functions in the central nervous system. However, whether these statins can affect cholesterol levels and synaptic plasticity in hippocampus and the in vivo consequence remain unclear. Here, we report that long-term subcutaneous treatments of simvastatin significantly impair mouse hippocampal synaptic plasticity, reflected by the attenuated long-term potentiation of field excitatory postsynaptic potentials. The simvastatin administration causes a

deficiency in recognition and spatial memory but fails to affect motor ability and anxiety behaviors in the mice. Mass spectrometry imaging indicates a significant decrease in cholesterol intensity in hippocampus of the mice receiving chronic simvastatin treatments. Such effects of simvastatin are transient because drug discontinuation can restore the hippocampal cholesterol level and synaptic plasticity and the memory function. These findings may provide further clues to elucidate the mechanisms of neurological side effects, especially the brain cognitive function impairment, caused by long-term usage of BBB-permeable statins.

[46] *Alshogran OY, Nusair SD, El-Elimat T et al.* **Evaluation of coenzyme Q10 combined with or without N-acetyl cysteine or atorvastatin for preventing contrast-induced kidney injury in diabetic rats**. Naunyn-Schmiedeberg's archives of pharmacology 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33630121
ABSTRACT
Combined antioxidants effect for prevention of contrast-induced nephropathy (CIN) remains unclear. This study assessed the potential protective effects of coenzyme Q10 (CoQ10) alone or combined with N-acetyl cysteine (NAC) or atorvastatin against CIN in diabetic rats. Animals were randomly divided into five groups, including control and four disease groups with CIN and diabetes. Group 2 included diabetic rats with CIN. Groups 3-5 included diabetic rats that received CoQ10, CoQ10 and NAC, or CoQ10 and atorvastatin, respectively, before CIN induction. Serum, urine, and tissue were collected to evaluate renal protective effects of tested agents. Renal biomarkers, oxidative stress, and histopathological alterations were investigated. Rats with CIN showed significant renal impairment as revealed by the deleterious effects on kidney function and histology. While induction of CIN did not affect the renal levels of catalase, glutathione peroxidase (GPx), and thiobarbituric acid reactive substances, pretreatment of animals with CoQ10/NAC showed significant increase in GPx and catalase levels versus controls. Lastly, pretreatment with CoQ10/atorvastatin showed regenerative effect on distal tubules with mild kidney histology alterations relative to CIN rats. The combined use of CoQ10/atorvastatin could be a potential strategy to prevent CIN. However, future studies are warranted to test different combinations for longer prophylactic periods.

[47] *Guo Y, Zhang YG, Li HC, Xu YH*. **Transiently Elevated TC and sdLDL-C Levels and Falsely Low LDL-C Levels in Patients with Extrahepatic Cholangiocarcinoma**. OncoTargets and therapy 2021; 14:1061-1071.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33623393
ABSTRACT
PURPOSE: Most patients diagnosed with extrahepatic cholangiocarcinoma (ECCA) exhibit cholestasis caused by obstruction of the bile duct. Cholestasis is associated with lipid disorders, but studies focused on the changing lipid parameters in patients with ECCA are lacking. Here, we observed lipid profiles in patients with ECCA and investigated whether the removal of biliary obstruction could correct dyslipidemia. PATIENTS AND METHODS: We consecutively included patients admitted to the hepatobiliary surgery department at the Affiliated Hospital of Xuzhou Medical University. The patients were divided into an ECCA group or a non-ECCA group based on the disease assessment. Patients with histological confirmation of ECCA were included in the ECCA group. Blood samples were collected on admission as well as five days after treatment. An automatic biochemistry analyzer was used to test liver function and serum lipid levels. Serum lipoprotein

electrophoresis was performed using barbitone sodium buffer and Sudan black B. RESULTS: A total of 180 patients met inclusion criteria and were enrolled for this study. Of these, 76 patients were diagnosed with ECCA; all other patients were enrolled in the non-ECCA group. Total cholesterol (TC) and small and dense low-density lipoprotein cholesterol (sdLDL-C) levels were significantly elevated in the ECCA group. LDL-C levels were found to be slightly lower in the ECCA group. In the ECCA group, serum samples were detained in sample wells and lipoproteins failed to be separated. TC and sdLDL-C levels significantly decreased after cholestasis relief in the ECCA group. Lipoprotein electrophoresis revealed that patients with ECCA showed normal lipoprotein patterns after treatment. CONCLUSION: Patients with ECCA exhibited transiently elevated TC and sdLDL-C levels and falsely low LDL-C results. TC, sdLDL-C, and LDL-C levels could be restored to normal levels after biliary obstruction removal and cholestasis relief.

[48] *Garside B, Ho JH, Kwok S et al.* **Changes in PCSK 9 and apolipoprotein B100 in Niemann-Pick disease after enzyme replacement therapy with olipudase alfa**. Orphanet journal of rare diseases 2021; 16:107.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33639994
ABSTRACT
BACKGROUND: Enzyme replacement therapy (ERT) with olipudase alfa, a recombinant human acid sphingomyelinase (rhASM), is being developed to treat patients with ASM deficiency (ASMD), commonly known as Niemann-Pick disease (NPD) types A or B. This study assessed the effect of ERT on lipid parameters and inflammatory markers. METHODS: Serum and plasma samples from five adults with NPD type B (NPD-B) who received olipudase alfa ERT for 26 weeks were analysed. We also collected fasting blood samples from fifteen age- and sex-matched participants as reference and comparison group. We measured fasting lipid profile, apolipoproteins B48 and B100 (apoB48 and apoB100), apolipoprotein A1 (apoA1), proprotein convertase subtilisin/klexin type 9 (PCSK9) mass, oxidised low-density lipoprotein (oxLDL), small dense low-density lipoprotein cholesterol (sdLDL-C) and tumour necrosis factor α (TNF-α). RESULTS: Patients with NPD-B, compared with age and sex matched reference group, had higher triglycerides, PCSK9, apoB48, oxLDL and TNF-α and lower high density lipoprotein cholesterol (HDL-C) and apoA1. Treatment with ERT was associated with improved lipid parameters including total cholesterol, triglycerides, low density lipoprotein cholesterol (LDL-C), sdLDL-C, oxLDL and apoB100. Though there was an increase in apoA1, HDL-C was slightly reduced. TNF-α showed a reduction. ApoB100 decreased in parallel with a decrease in total serum PCSK9 mass after ERT. CONCLUSION: This study demonstrated that patients with NPD-B had a proatherogenic lipid profile and higher circulating TNF-α compared to reference group. There was an improvement in dyslipidaemia after olipudase alfa. It was possible that reductions in LDL-C and apoB100 were driven by reductions in TNF-α and PCSK9 following ERT.

[49] *Víšek J, Bláha M, Bláha V et al.* **Monitoring of up to 15 years effects of lipoprotein apheresis on lipids, biomarkers of inflammation, and soluble endoglin in familial hypercholesterolemia patients**. Orphanet journal of rare diseases 2021; 16:110.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33640001
ABSTRACT
BACKGROUND: Lipoprotein apheresis (LA) is considered as an add-on therapy for patients with familial hypercholesterolemia (FH). We aimed to analyze the data collected in the last 15 years from

FH patients treated with LA, to elucidate the benefit of this procedure with respect to plasma lipids, biomarkers of inflammation, and endothelial dysfunction and soluble endoglin. RESULTS: 14 patients (10 heterozygous FH patients (HeFH), 4 homozygous FH patients (HoFH)) were treated by long-term lipoprotein apheresis. Lipid levels were examined, and ELISA detected biomarkers of inflammation and soluble endoglin. Paired tests were used for intergroup comparisons, and a linear regression model served to estimate the influence of the number of days patients were treated with LA on the studied parameters. LA treatment was associated with a significant decrease of total cholesterol (TC), LDL-C, HDL-C, and apoB, in both HeFH and HoFH patients, after single apheresis and in a long-term period during the monitored interval of 15 years. Biomarkers of inflammation and endothelial dysfunction were reduced for soluble endoglin, hsCRP, and MCP-1, and sP-selectin after each procedure in some HeFH and HoFH patients. CONCLUSIONS: LA treatment up to 15 years, reduced cholesterol levels, levels of biomarkers related to endothelial dysfunction, and inflammation not only after each procedure but also in the long-term evaluation in FH patients. We propose that long-term LA treatment improves lipid profile and endothelial dysfunction in familial hypercholesterolemia patients, suggesting a promising improvement in cardiovascular prognosis in most FH patients.

[50] *Nikniaz L, Abbasalizad-Farhangi M, Vajdi M, Nikniaz Z*. **The association between Sugars Sweetened Beverages (SSBs) and lipid profile among children and youth: A systematic review and dose-response meta-analysis of cross-sectional studies**. Pediatric obesity 2021:e12782.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33629539

ABSTRACT

BACKGROUND: The relationship between sugar-sweetened beverages (SSBs) intake and serum lipids among children and youth has been reported in several studies, but the results are still controversial. OBJECTIVE: In the current study, we summarized the results of studies that assessed the relationship between SSBs consumption and serum lipids among children and youth in a systematic review and dose-response meta-analysis. METHODS: The PubMed, Web of Sciences, Cochrane and Scopus electronic databases were searched for observational studies reporting an association between SSBs intake and serum lipids among children and youth that were published before May 2020. For data extracted from cohort studies, only cross-sectional baseline data were included in the current meta-analysis. The Random effects model was used to estimate the pooled weighted mean difference (WMD) and 95% confidence intervals (CI). Heterogeneity was assessed with the Cochran Q test and I(2) statistics. RESULTS: In our search, 1845 studies were retrieved of which 13 studies (two cohorts and eleven cross-sectional) were included. High SSB consumption was associated with 1.21 mg/dL increase in low-density lipoprotein cholesterol (LDL-C; pooled WMD: 1.21 mg/dL; 95% CI: 0.23, 2.20; P = .01), 1.45 mg/dL decrease in high-density lipoprotein cholesterol (HDL-C, pooled WMD: -1.46 mg/dL; 95% CI, -2.25, -0.67; P < .0001) and 2.49 mg/dL decrease in total cholesterol (TC, pooled WMD: -2.49 mg/dL; 95% CI, -2.89, -2.10; P < .0001). In dose-response meta-analysis, there was an evidence of departure from linearity in the relationship between SSB consumption and change in LDL-C (P-(nonlinearity) = .03) and TC (P-(nonlinearity) = .01). However, no departure from linearity was observed between SSB intake and change in HDL-C (P-(nonlinearity) = .56) or triglyceride (TG) values (P-(nonlinearity) = .85). CONCLUSION: According to our results, high SSB consumption was significantly associated with higher LDL-C and lower HDL-C and TC among children and youth. However, owing to the limited number of the included studies, further well-designed interventional studies are needed to better elucidate causality.

[51] *Kim J, Kim HS, Bae YJ et al.* **Comparing different types of statins for secondary prevention of cardio-cerebrovascular disease from a national cohort study**. PloS one 2021; 16:e0247419.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33630898
ABSTRACT
Statins have been recommended for use in atherosclerotic cardio-cerebrovascular disease (CCVD). The purpose of this study was to investigate the efficacy of five different types of statin in the secondary prevention of CCVD in patients. This study retrospectively designed and analyzed data from the National Health Insurance Service-National Health in Korea. Participants aged 40 to 69 years were categorized into five statin groups (atorvastatin, rosuvastatin, pitavastatin, simvastatin, and pravastatin). The primary composite outcome was defined as recurrence of CCVD or all causes of death. Cox proportional hazard regression models were adopted after stepwise adjustments for confounders to investigate the difference in efficacy among the different statins. Of the 755 final participants, 48 patients experienced primary composite outcomes. After adjustments, the hazard ratios (95% confidence intervals) for primary composite outcomes of atorvastatin, pitavastatin, and rosuvastatin groups were 0.956 (0.456-2.005), 1.347 (0.354-5.116), and 0.943 (0.317-2.803), respectively, when compared with the simvastatin group. There were no significant differences between the statins in efficacy for preventing recurrence of CCVD events and/or death in CCVD patients.

[52] *Parsamanesh N, Karami-Zarandi M, Banach M et al.* **Effects of statins on myocarditis: A review of underlying molecular mechanisms**. Prog Cardiovasc Dis 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33621589
ABSTRACT
Myocarditis refers to the clinical and histological characteristics of a diverse range of inflammatory cellular pathophysiological conditions which result in cardiac dysfunction. Myocarditis is a major cause of mortality in individuals less than 40 years of age and accounts for approximately 20% of cardiovascular disease (CVD) events. Myocarditis contributes to dilated cardiomyopathy in 30% of patients and can progress to cardiac arrest, which has a poor prognosis of <40% survival over 10 years. Myocarditis has also been documented after infection with SARS-CoV-2. The most commonly used lipid-lowering therapies, HMG-CoA reductase inhibitors (statins), decrease CVD-related morbidity and mortality. In addition to their lipid-lowering effects, increasing evidence supports the existence of several additional beneficial, 'pleiotropic' effects of statins. Recently, several studies have indicated that statins may attenuate myocarditis. Statins modify the lipid oxidation, inflammation, immunomodulation, and endothelial activity of the pathophysiology and have been recommended as adjuvant treatment. In this review, we focus on the mechanisms of action of statins and their effects on myocarditis, SARS-CoV-2 and CVD.

[53] *Silvino JPP, Carvalho MG, Reis EA et al.* **Familial hypercholesterolemia: Is there a role for PCSK9 and thrombin generation?** Thrombosis research 2021; 200:156-163.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33626480
ABSTRACT
INTRODUCTION: Familial hypercholesterolemia (FH) is an autosomal dominant genetic disease. The prevalence of FH has previously been reported as 1 in 500 in the general population. This study

aimed to evaluate the proprotein convertase subtilisin/kexin 9 (PCSK9) levels, lipid profile and thrombin generation in FH patients undergoing treatment or not. METHODS: Eighty individuals with FH were selected and distributed in 2 groups: individuals treated with statins alone or conjugate therapy (statin + ezetimibe) (T = 53) and those non treated (NT = 27). PCSK9 levels were determined by ELISA, the lipid profile by colorimetric enzyme method and thrombin generation assay (TGA) by CAT method. RESULTS: Individuals treated with conjugate therapy (statin + ezetimibe) showed a significant reduction in the levels of total cholesterol (TC) low density lipoprotein cholesterol (LDLc) and in the potential for thrombin generation (ETP with low and high concentration of tissue factor), compared to the treated individuals with monotherapy (statins). PCSK9 was positively correlated with increased levels of TC, LDLc and triglycerides, while TGA parameters were positively correlated with PCSK9 and lipid profile. CONCLUSION: PCSK9 levels appear to be associated with components of the lipid and hemostatic profiles, in addition to being influenced by age. In general, our findings suggest that combined therapy for the treatment of FH is associated with a significant improvement in both lipid and hemostatic profiles assessed by TGA, suggesting a reduction in atherogenic and thrombogenic risks and, therefore, more promising compared to the use of statin monotherapy.

[54] *Ravikanth R*. **Role of (18)F-FDG positron emission tomography in carotid atherosclerotic plaque imaging: A systematic review**. World J Nucl Med 2020; 19:327-335.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33623500

ABSTRACT

Stroke and other thromboembolic events in the brain are often due to carotid artery atherosclerosis, and atherosclerotic plaques with inflammation are considered particularly vulnerable, with an increased risk of becoming symptomatic. Positron emission tomography (PET) with 2-deoxy-2-[Fluorine-18] fluoro-D-glucose ((18)F-FDG) provides valuable metabolic information regarding arteriosclerotic lesions and may be applied for the detection of vulnerable plaque. At present, however, patients are selected for carotid surgical intervention on the basis of the degree of stenosis alone, and not the vulnerability or inflammation of the lesion. During the past decade, research using PET with the glucose analog tracer (18)F-fluor-deoxy-glucose, has been implemented for identifying increased tracer uptake in symptomatic carotid plaques, and tracer uptake has been shown to correlate with plaque inflammation and vulnerability. These findings imply that (18)F-FDG PET might hold the promise for a new and better diagnostic test to identify patients eligible for carotid endarterectomy. The rationale for developing diagnostic tests based on molecular imaging with (18)F-FDG PET, as well as methods for simple clinical PET approaches, are discussed. This is a systematic review, following Preferred Reporting Items for Systematic Reviews guidelines, which interrogated the PUBMED database from January 2001 to November 2019. The search combined the terms, "atherosclerosis," "inflammation," "FDG," and "plaque imaging." The search criteria included all types of studies, with a primary outcome of the degree of arterial vascular inflammation determined by (18)F-FDG uptake. This review examines the role of (18)F-FDG PET imaging in the characterization of atherosclerotic plaques.