[1] *Rao W, Zhang Y, Li K, Zhang XY*. **Association between cognitive impairment and apolipoprotein A1 or apolipoprotein B levels is regulated by apolipoprotein E variant rs429358 in patients with chronic schizophrenia**. Aging 2021; 13:16353-16366.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34135129

ABSTRACT

ApoE gene polymorphism may be involved in the change in blood lipid profile and cognitive impairment of the general population. However, few studies explored the effects of ApoE gene polymorphism on blood lipid levels and cognition in schizophrenia. The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) was employed to evaluate the cognition and the SNPStats was used to investigate the association of ApoE rs429358 with schizophrenia. The models of analysis of covariance and multivariate analysis were conducted to investigate the effect of ApoE rs429358 on cognition in schizophrenia. Altogether, 637 patients with schizophrenia and 467 healthy controls were recruited in this study. The findings in the case group found that both the ApoA1 and ApoB levels were predictors for RBANS total score ($p < 0.001$ vs. $p = 0.011$), immediate memory ($p < 0.001$ vs. $p = 0.019$), language ($p < 0.001$ vs. $p = 0.013$), attention ($p < 0.001$ vs. $p < 0.001$), except ApoA1 level only was a predictor for visuospatial/constructional ($p = 0.014$) and delayed memory ($p < 0.001$). When the association was examined in different ApoE rs429358 genotype subgroups, the association between ApoA1 level and RBANS scores (except for the language score) or between ApoB level and RBANS scores (except for the attention score) was regulated by ApoE rs429358. Our results suggest that patients with schizophrenia have broad cognitive impairment compared with healthy controls. For patients with schizophrenia, both ApoA1 and ApoB levels were positively associated with cognition. There was a significant association between ApoA1 or ApoB levels and cognition in schizophrenia, which was regulated by the ApoE rs429358.

[2] *Khan R, Kaul P, Islam S et al.* **Drug Adherence and Long-Term Outcomes in Non-Revascularized Patients Following Acute Myocardial Infarction**. The American journal of cardiology 2021; 152:49-56.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34120704

ABSTRACT

This study examined long-term outcomes and adherence to guideline-based medications in non-revascularized acute myocardial infarction (MI) patients undergoing and not undergoing angiography. We analyzed non-revascularized MI patients hospitalized in Alberta, Canada between 2010-2016 and categorized them according to whether they had undergone coronary angiography. Adherence to guideline-based medications was determined by the proportion of days covered (PDC) and subdivided into categories based on PDC: 0% (none), 1-40% (low), 40-79% (intermediate) and ≥ 80% (high). Patients not undergoing angiography were older, less frequently male, and had more comorbidities. Those not receiving angiography had higher rates of 2-year myocardial infarction (9.9% vs 6.1%, $p <0.001$), heart failure (14.9% vs 6.1%, $p <0.001$), and mortality (29.4% vs 7.4%, $p <0.001$). Optimal medial therapy (OMT), defined by high PDC for the combination of lipid-modifying agents, β-blockers and angiotensin converting enzyme-inhibitors/receptor blockers (ACE-I/ARBs), was achieved in 32.9%. Patients not undergoing angiography had lower rates of OMT adherence ($p <0.001$). In patients not undergoing angiography, high-adherence to lipid-modifying agents (HR 0.70 [95% CI 0.57-0.87]), β-blockers (HR 0.78 [0.62-0.97]), ACE-I/ARBs (HR 0.64 [0.52-0.79]) and OMT (HR 0.56 [0.40-0.77]) was independently associated with lower 2-year mortality. In conclusion, MI

patients not receiving angiography had low adherence rates to guideline-based pharmacotherapies and high rates of long-term outcomes, suggesting potential treatment targets to improve prognosis in non-invasively managed MI patients.

[3] *Ronsein GE, Vaisar T, Davidson WS et al.* **Niacin Increases Atherogenic Proteins in High-Density Lipoprotein of Statin-Treated Subjects**. Arteriosclerosis, thrombosis, and vascular biology 2021; 41:2330-2341.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34134520
ABSTRACT
[Figure: see text].

[4] *Shibutani H, Fujii K, Ueda D et al.* **Automated classification of coronary atherosclerotic plaque in optical frequency domain imaging based on deep learning**. Atherosclerosis 2021; 328:100-105.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34126504
ABSTRACT
BACKGROUND AND AIMS: We developed a deep learning (DL) model for automated atherosclerotic plaque categorization using optical frequency domain imaging (OFDI) and performed quantitative and visual evaluations. METHODS: A total of 1103 histological cross-sections from 45 autopsy hearts were examined to compare the ex vivo OFDI scans. The images were segmented and annotated considering four histological categories: pathological intimal thickening (PIT), fibrous cap atheroma (FA), fibrocalcific plaque (FC), and healed erosion/rupture (HER). The DL model was developed based on pyramid scene parsing network (PSPNet). Given an input image, a convolutional neural network (ResNet50) was used as an encoder to generate feature maps of the last convolutional layer. RESULTS: For the quantitative evaluation, the mean F-score and IoU values, which are used to evaluate how close the predicted results are to the ground truth, were used. The validation and test dataset had F-score and IoU values of 0.63, 0.49, and 0.66, 0.52, respectively. For the section-level diagnostic accuracy, the areas under the receiver-operating characteristic curve produced by the DL model for FC, PIT, FA, and HER were 0.91, 0.85, 0.86, and 0.86, respectively, and were comparable to those of an expert observer. CONCLUSIONS: DL semantic segmentation of coronary plaques in OFDI images was used as a tool to automatically categorize atherosclerotic plaques using histological findings as the gold standard. The proposed method can support interventional cardiologists in understanding histological properties of plaques.

[5] *Bhattacharya A, Chowdhury A, Chaudhury K, Shukla PC*. **Proprotein convertase subtilisin/kexin type 9 (PCSK9): A potential multifaceted player in cancer**. Biochim Biophys Acta Rev Cancer 2021; 1876:188581.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34144130
ABSTRACT
Proprotein convertase subtilisin/kexin type 9 (PCSK9) has emerged as a novel pharmacological target for hypercholesterolemia and associated cardiovascular diseases owing to its function to mediate the degradation of low-density lipoprotein receptor (LDLR). Findings over the past two decades have identified novel binding partners and cellular functions of PCSK9. Notably, PCSK9 is aberrantly expressed in a broad spectrum of cancers and apparently contributes to disease

prognosis, indicating that PCSK9 could be a valuable cancer biomarker. Experimental studies demonstrate the contribution of PCSK9 in various aspects of cancer, including cell proliferation, apoptosis, invasion, metastasis, anti-tumor immunity and radioresistance, strengthening the idea that PCSK9 could be a promising therapeutic target. Here, we comprehensively review the involvement of PCSK9 in cancer, summarizing its aberrant expression, association with disease prognosis, biological functions and underlying mechanisms in various malignancies. Besides, we highlight the potential of PCSK9 as a future therapeutic target in personalized cancer medicine.

[6] *Smith W, Cheng-Lai A, Nawarskas J.* **Bempedoic Acid: A New Avenue for the Treatment of Dyslipidemia**. Cardiology in review 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34132656
ABSTRACT
Uncontrolled dyslipidemia, specifically elevation of low density lipoprotein cholesterol, is a major risk factor for developing cardiovascular disease. Currently, statin therapy remains first line treatment for reducing both serum cholesterol levels and cardiovascular risk. However, certain patients are unable to achieve desired serum cholesterol levels despite maximally tolerated statin therapy. As a result, several non-statin therapy avenues have been evaluated for their potential benefits in reducing cholesterol and cardiovascular risk. Bempedoic acid is one such non-statin therapy option which has been explored over the past few years to potentially assist patients in further reducing serum cholesterol. Bempedoic acid is a novel prodrug that inhibits cholesterol synthesis upstream of statins by inhibiting adenosine triphosphate-citrate lyase. Bempedoic acid has been studied as a single, once daily 180 mg dose. Administered as monotherapy or in combination with statin or ezetimibe, bempedoic acid significantly reduces low density lipoprotein cholesterol. Furthermore, bempedoic acid was generally well tolerated by patients and rates of adverse events were similar to placebo with few exceptions. Despite proven reductions in cholesterol and favorable safety profile, bempedoic acid will likely remain a third- or fourth-line agent for the treatment of dyslipidemia behind other non-statin therapies until improvement of cardiovascular outcomes is demonstrated in future clinical trials.

[7] *Nakagawa I, Kotsugi M, Park H et al.* **Lipid Core Burden Index Assessed by Near-Infrared Spectroscopy of Symptomatic Carotid Plaques: Association with Magnetic Resonance T1-Weighted Imaging**. Cerebrovasc Dis 2021:1-8.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34148038
ABSTRACT
INTRODUCTION: Vulnerable plaques are a strong predictor of cerebrovascular ischemic events, and high lipid core plaques (LCPs) are associated with an increased risk of embolic infarcts during carotid artery stenting (CAS). Recent developments in magnetic resonance (MR) plaque imaging have enabled noninvasive assessment of carotid plaque vulnerability, and the lipid component and intraplaque hemorrhage (IPH) are visible as high signal intensity areas on T1-weighted MR images. Recently, catheter-based near-infrared spectroscopy (NIRS) has been shown to accurately distinguish LCPs without IPH. This study aimed to determine whether the results of assessment of high LCPs by catheter-based NIRS correlate with the results of MR plaque imaging. METHODS: We recruited 82 consecutive symptomatic carotid artery stenosis patients who were treated with CAS under NIRS and MR plaque assessment. Maximum lipid core burden index (max-LCBI) at minimal luminal areas (MLA), defined as max-LCBIMLA, and max-LCBI for any 4-mm segment in a target

lesion, defined as max-LCBIAREA, were assessed by NIRS. Correlations were investigated between max-LCBI and MR T1-weighted plaque signal intensity ratio (T1W-SIR) and MR time-of-flight signal intensity ratio (TOF-SIR) in the same regions as assessed by NIRS. RESULTS: Both T1W-SIRMLA and T1W-SIRAREA were significantly lower in the high LCP group (max-LCBI >504, $p < 0.001$ for both), while TOF-SIRMLA and TOF-SIRAREA were significantly higher in the high LCP group ($p < 0.001$ and $p = 0.004$, respectively). A significant linear correlation was present between max-LCBIMLA and both TIW-SIRMLA and TOF-SIRMLA ($r = -0.610$ and 0.452, respectively, $p < 0.0001$ for both). Furthermore, logistic regression analysis revealed that T1W-SIRMLA and TOF-SIRMLA were significantly associated with a high LCP assessed by NIRS (OR, 44.19 and 0.43; 95% CI: 6.55-298.19 and 0.19-0.96; $p < 0.001$ and $= 0.039$, respectively). CONCLUSIONS: A high LCP assessed by NIRS correlates with the signal intensity ratio of MR imaging in symptomatic patients with unstable carotid plaques.

[8] *Levin MG, Zuber V, Walker VM et al.* **Prioritizing the Role of Major Lipoproteins and Subfractions as Risk Factors for Peripheral Artery Disease**. Circulation 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34139859

ABSTRACT

Background: Lipoprotein-related traits have been consistently identified as risk factors for atherosclerotic cardiovascular disease, largely on the basis of studies of coronary artery disease (CAD). The relative contributions of specific lipoproteins to risk of peripheral artery disease (PAD) have not been well-defined. We leveraged large-scale genetic association data to investigate effects of circulating lipoprotein-related traits on PAD risk. Methods: Genome-wide association study summary statistics for circulating lipoprotein-related traits were used in the MR Bayesian model averaging framework to prioritize the most likely causal major lipoprotein and subfraction risk factors for PAD and CAD. MR was used to estimate the effect of ApoB-lowering on PAD risk using gene regions proxying lipid-lowering drug targets. Genes relevant to prioritized lipoprotein subfractions were identified using transcriptome-wide association studies. Results: ApoB was identified as the most likely causal lipoprotein-related risk factor for both PAD (marginal inclusion probability [MIP] 0.86, $p = 0.003$) and CAD (MIP 0.92, $p = 0.005$). Genetic proxies for ApoB (apolipoprotein B)-lowering medications were associated with reduced risk of both PAD (OR 0.87 per 1 standard deviation decrease in ApoB, 95% CI 0.84 to 0.91, $p = 9 \times 10(-10)$) and CAD (OR 0.66, 95% CI 0.63 to 0.69, $p = 4 \times 10(-73)$), with a stronger predicted effect of ApoB-lowering on CAD (ratio of effects 3.09, 95% CI 2.29 to 4.60, $p < 1 \times 10(-6)$). Extra-small-VLDL particle concentration (XS.VLDL.P) was identified as the most likely subfraction associated with PAD risk (MIP 0.91, $p = 2.3 \times 10(-4)$), while large-LDL particle concentration (L.LDL.P) was the most likely subfraction associated with CAD risk (MIP 0.95, $p = 0.011$). Genes associated with XS.VLDL.P and L.LDL.P included canonical ApoB-pathway components, although gene-specific effects were variable. Lipoprotein(a) was associated with increased risk of PAD, independent of ApoB (OR 1.04, 95% CI 1.03 to 1.04, 95% CI $1.0 \times 10(-33)$). Conclusions: ApoB was prioritized as the major lipoprotein fraction causally responsible for both PAD and CAD risk. However, ApoB-lowering drug targets and ApoB-containing lipoprotein subfractions had diverse associations with ASCVD, and distinct subfraction-associated genes suggest possible differences in the role of lipoproteins in the pathogenesis of PAD and CAD.

[9] *Erol SA, Tanacan A, Firat Oguz E et al.* **A comparison of the maternal levels of serum proprotein convertase subtilisin/kexin type 9 in pregnant women with the complication of fetal open neural tube defects**. Congenit Anom (Kyoto) 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34128273
ABSTRACT
It was aimed to evaluate the levels of maternal serum proprotein convertase subtilisin/kexin type 9 (PCSK9) in pregnant women with a fetus diagnosed with open neural tube defects (NTDs). This case-control study included 38 pregnant women carrying fetuses with open NTDs and 44 age-matched, pregnant women with no specified risk factors. Comparisons were made of the groups in respect of demographic and clinical data and PCSK9 levels. To examine the performance of PCSK9 levels in the prediction of fetal open NTDs, receiver operating characteristic (ROC) curve analysis was used. In the first and second trimesters, PCSK9 levels were determined to be lower in the NTD group than in the control group ($p = 0.010$ and $p = 0.015$, respectively). In the first trimester, the lower PCSK9 levels in the NTD group were not statistically significant ($p = 0.575$). In the second trimester, the ROC curve value with the best balance of sensitivity/specificity for PCSK9 was 71.9 ng/ml (84.6% sensitivity, 51.7% specificity) and in the first and second trimester combined, 74.4 ng/ml (81.6% sensitivity, 45.5% specificity) ($p = 0.015$, $p = 0.036$, respectively). PCSK9 may be involved in the etiopathogenesis of open NTDs at the critical steps of fetal neuronal differentiation. Although it has limitations, PCSK9 may be used as an additional biomarker for the screening of NTDs.

[10] *Agarwala A, Goldberg A.* **Special Considerations for Lipid-Lowering Therapy in Women Reflecting Recent Randomized Trials**. Current atherosclerosis reports 2021; 23:42.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34146167
ABSTRACT
PURPOSE OF REVIEW: Atherosclerotic cardiovascular disease (ASCVD) is the leading cause of mortality in women across all racial and ethnic groups within the USA. Despite robust evidence from randomized controlled trials demonstrating that treatment of hypercholesterolemia in women reduces cardiovascular events, women who are eligible for lipid-lowering therapy are less likely than men to be prescribed guideline-recommended therapy or to have therapy prescribed at the appropriate intensity. RECENT FINDINGS: Historically, women have been underrepresented in clinical trials. Recent randomized clinical trials have shown that women derive similar benefits as men when treated with lipid-lowering therapy, and recent studies demonstrate potential uses for lipid-lowering therapies that extend beyond their previously well-established indications. In this review, we will discuss lipid-lowering therapies in the context of recent clinical trials with a focus on special considerations in women.

[11] *Miname MH, Rocha VZ, Santos RD.* **The Role of RNA-Targeted Therapeutics to Reduce ASCVD Risk: What Have We Learned Recently?** Current atherosclerosis reports 2021; 23:40.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34146170
ABSTRACT
PURPOSE OF REVIEW: To discuss advances on the RNA-targeted therapies to treat dyslipidemia with the aim of reducing atherosclerotic cardiovascular disease (ASCVD). RECENT FINDINGS: Genetic studies have paved the way for therapies that reduce translation of proteins that play causal roles in dyslipidemia and atherosclerosis like proprotein convertase subtilisin/kexin type 9 (PCSK9),

apolipoprotein B-100 (apoB), apolipoprotein(a) [apo(a)], apolipoprotein C3 (apoC3), and angiopoietin-like 3 (ANGPTL3). Either antisense oligonucleotide (ASO) therapies and small interfering RNA (siRNA) molecules inhibit protein synthesis and consequently improve dyslipidemia. Most of these molecules contain N-acetylgalactosamine (GalNAc) moieties that have high specificity for hepatocytes and therefore reduce concentration in other tissues. Inclisiran, an siRNA for PCSK9, has shown robust LDL-C reductions, with good tolerability, in severe forms of hypercholesterolemia as well as in high cardiovascular disease patients with injections every 3 to 6 months. Pelacarsen is an ASO against apolipoprotein(a) that reduces Lp(a) up to 80% with good tolerability. Either inclisiran or pelacarsen is being tested to show it can prevent ASCVD. AMG 890, an siRNA compound aimed at reducing apo(a) synthesis, is also under investigation. Volanesorsen is an ASO against apoC3 that reduces triglyceride levels up to 70% and is being tested in severe hypertriglyceridemic patients. Vupanorsen is an ASO against ANGPTL3 that reduced triglyceride levels 36-53% among moderate hypertriglyceridemic individuals. Interestingly, it also reduces ApoC3 and non-HDL cholesterol and apoB; however, it lowers HDL cholesterol. RNA-targeted therapies are being extensively tested for dyslipidemia treatment with promising results.

[12] *Ruotsalainen AK, Mäkinen P, Ylä-Herttuala S*. **Novel RNAi-Based Therapies for Atherosclerosis**. Current atherosclerosis reports 2021; 23:45.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34146172

ABSTRACT

PURPOSE OF REVIEW: Atherosclerosis, defined by inflammation and accumulation of cholesterol, extracellular matrix, and cell debris into the arteries is a common factor behind cardiovascular diseases (CVD), such as coronary artery disease, peripheral artery disease, and stroke. In this review, we discuss and describe novel RNA interference (RNAi)-based therapies in clinical trials and on the market. RECENT FINDINGS: The first RNAi-based therapies have entered clinical use for the control of atherosclerosis risk factors, i.e., blood cholesterol levels. The most advanced treatment is silencing of proprotein convertase subtilisin/kexin type 9 (PCSK9) with a drug called inclisiran, which has been approved for the treatment of hypercholesterolemia in late 2020, and results in a robust decrease in plasma cholesterol levels. As the new RNAi therapies for atherosclerosis are now entering markets, the usefulness of these therapies will be further evaluated in larger patient cohorts. Thus, it remains to be seen how fast, effectively and eminently these new drugs consolidate their niche within the cardiovascular disease drug palette.

[13] *Ellulu MS, Naser IA, Abuhajar SM, Najim AA*. **Determination of risk factors associated with inflammation in hypertensive patients with type-2 diabetes mellitus in a Palestinian Diabetes Study**. Current medical research and opinion 2021:1-9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34125641

ABSTRACT

OBJECTIVE: To determine the risk factors associated with inflammation in hypertensive patients with type-2 diabetes mellitus. METHODS: A total of 164 hypertensive patients with type 2 diabetes patients aged 38-60 years were selected from 7 primary healthcare centers in Gaza city, Palestine. Interview questionnaire were employed to collect data related to age, gender, smoking habits, and physical activity pattern. Laboratory biochemical tests included fasting blood glucose (FBG), triglyceride (TG), total cholesterol (TC), interleukin 6 (IL-6), high sensitive C reactive protein (hs-

CRP), and adiponectin were estimated in all patients. RESULTS: The study involved 118 (72%) women and 46 (28%) men; the mean of age was 53.7 ± 0.46 years. A tertile of inflammation feature with hs-CRP was developed. The highest tertile of hs-CRP was significantly associated with women, higher obesity indices, metabolic dysregulation involving lipid profile markers, FBG and blood pressure, IL-6, and lower adiponectin. After adjusting for age, gender, smoking habits, and physical activity; the risk factor of high level of hs-CRP were the increased body mass index [OR: 1.17, p = .018], IL-6 [OR: 2.22, p = .025] and FBG [OR: 1.01, p = .007], as well as reduced adiponectin [OR: 0.81, p = .002]. CONCLUSION: The inflammation state was affected by obesity and had been related to altered adipokines levels of IL-6 and adiponectin, as well as affected by the glycemic control, as evidenced by higher serum level of FBG.

[14] *Eikelboom R, Amir T, Gupta S, Whitlock RP*. **Optimal medical therapy after coronary artery bypass grafting: a primer for surgeons**. Current opinion in cardiology 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34138766
ABSTRACT
PURPOSE OF REVIEW: After coronary artery bypass grafting (CABG), patients remain at increased risk of cardiovascular events and death. Cardiac surgeons have the opportunity to reduce this risk by optimizing post-CABG patients' medical therapy. RECENT FINDINGS: Recent developments in lipid-lowering, diabetes management, antithrombotic therapy, and anti-inflammatory therapy can significantly improve prognosis in patients with chronic coronary artery disease. PCSK-9 inhibitors should be used in patients with elevated LDL cholesterol despite maximally tolerated statin therapy. Icosapent ethyl should be considered in patients with elevated triglycerides despite maximally tolerated statin therapy. Long-acting GLP-1 receptor agonists or SLGT-2 inhibitors should be used in all post-CABG patients with type 2 diabetes. Intensified antithrombotic therapy with DAPT or DPI reduces MACE (and DPI reduces mortality) in patients with high atherosclerotic burden. Colchicine has not yet been incorporated into guidelines on OMT for stable CAD but it is reasonable to consider using it in high-risk patients. SUMMARY: We review the foundations of optimal medical therapy after CABG, and summarize recent advances with a focus on practical application for the busy cardiac surgeon.

[15] *Amer MS, Hamza SA, Shaltoot HM et al.* **Interaction between apolipoprotein E genotyping, serum inflammatory biomarkers and cognitive functions in Egyptian elderly**. The Egyptian journal of immunology 2021; 28:1-11.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34147049
ABSTRACT
There is evidence consistent with the hypothesis that genetic, inflammatory and immune mechanisms are involved in the pathogenesis of AD. The aim of this study is to assess the relationship between Apolipoprotein E (Apo E), serum levels of inflammatory markers, and cognitive functions among elderly patients with Alzheimer's disease (AD) and Mild cognitive impairment (MCI) compared to elderly with normal cognitive function. 88 participants (≥60 years) from Ain Shams University Hospital were enrolled. They were divided into 3 groups: Group A (32 elderly patients with AD), Group B (32 elderly patients with MCI) and Group C (24 controls with normal cognitive function). All participants were subjected to comprehensive geriatric assessment, Apo E genotyping, measurement of C-reactive protein (CRP) and Alpha-1-antichymotrypsin (ACT), by PCR-RFLP, ELIZA and semi-

quantitative method respectively. The most common variant of Apo E gene was E3/E3 being more frequent in healthy control group (HC) than the other two groups and the least common variant was E4/E4 detected only in the AD group. ApoE4 allele was associated with 40.6% of AD patients (where 31.4% were heterozygous and 8.6 % homozygous) and 17.1% of MCI patients, whereas ApoE2 was more prevalent in the control group ($P<0.05$). A significant difference was observed when Mini mental status Examination (MMSE) score in different Apo E alleles was compared ($P<0.01$). The highest score was associated with (E2/E3) allele whereas, the lowest score was associated with (E4/E4) allele. Regarding inflammatory markers; CRP levels showed a statistically significant difference between the 3 groups and were higher in the AD group than the other 2 groups. ($P<0.01$). There was no statistically significant difference between the 3 groups as regard ACT level ($P>0.05$). Carriers of at least one E4 allele showed great risk to develop AD when combined with high CRP serum levels (OR = 36; CI: 11.4-113.7; $P< 0.01$). In conclusion, Apo E together with CRP may be a useful tool to predict Alzheimer's disease.

[16] *Irshad K, Akash MSH, Rehman K, Sharif H*. **Therapeutic interventions of novel SGLT2 inhibitors against metabolic disorders: inserting the association into perspectives**. Endocrine, metabolic & immune disorders drug targets 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34139987

ABSTRACT

Sodium-glucose co-transporter 2 (SGLT2) inhibitors are an emerging group of therapeutic agents that showcase their tremendous glucose-lowering activity without causing hypoglycemia, which is one of the major drawbacks of existing antidiabetic therapy. Comprehensive literature was searched in English language using electronic databases, including PubMed, ScienceDirect, Medline, Scopus, and Embase. SGLT2 inhibitors reduce blood glucose levels by causing glucosuria via an insulin-independent pathway. The major mechanism by which SGLT2 inhibitors are involved in glucose homeostasis is to prevent the reabsorption of glucose in the proximal convoluted tubule and increase glucose excretion in the urine. Deterioration of β-cells, impairment of functions, and development of insulin resistance do not affect the efficacy of SGLT2 inhibitors. SGLT2 inhibitors significantly reduce HbA1c, ameliorate glycemic control, and control body weight. SGLT2 inhibitors can block Na+/H+ exchanger (NHE) 1 and play a significant role in the treatment of heart failure, especially in diabetic patients. They also have positive effects on different metabolic syndromes, which cumulatively ameliorate the risk factors for cardiovascular diseases in diabetic patients. SGLT2 inhibitors can improve kidney function by reducing inflammation and improving renal microvasculature up to its original state. The increase in triglyceride level has a strong relationship with coronary artery disease in diabetic patients when combined with other indicators of metabolic disorders, while SGLT2 inhibitors cause a significant reduction in plasma triglyceride levels in diabetic patients. We have comprehensively summarized the features, mechanism of action of SGLT2 inhibitors, and their impact on various metabolic syndromes, including diabetic condition, renal dysfunctioning, arterial stiffness, hypertension, lipid profile, and cardiovascular diseases. This review aimed to examine the safety, efficacy, and therapeutic properties of SGLT2 inhibitors in renal and diabetic patients.

[17] *Coussa A, Hasan HA, Barber TM*. **Early Predictors of Gestational Diabetes Mellitus in IVF-Conceived Pregnancies**. Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists 2021; 27:579-585.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34120700
ABSTRACT
OBJECTIVE: Gestational diabetes mellitus (GDM) is associated with adverse maternal and fetal outcomes. This study aimed to identify early and reliable GDM predictors that would enable implementation of preventive and management measures. METHODS: The participants were a 28-week prospective cohort of in vitro fertilization (IVF)-conceived pregnant women (≤39 years, body mass index [BMI] 18.5-38 kg/m(2)) without a known history of diabetes mellitus. Fasting blood samples were analyzed at baseline (pre-IVF) and 12 weeks' gestation for reproductive hormones, glucose, serum insulin, lipids, thyroid function, adiponectin, and lipopolysaccharide-binding protein. At 28 weeks, a 75-g oral glucose tolerance test was used to screen for GDM. RESULTS: For the overall group at baseline, 22% had BMI ≥30 kg/m(2), 45% had polycystic ovary syndrome, 16% had hemoglobin A1C of 5.7% to 6.1%, and 14% had a past history of GDM. At 28 weeks of gestation (n = 158), 34 women had developed GDM and 124 had not. Significant baseline predictors of GDM onset included greater BMI (29.0 vs 25.8 kg/m(2)), older age (34 vs 32 years), higher levels of follicle-stimulating hormone/luteinizing hormone ratio (1.2 vs 1.0), hemoglobin A1C (5.5 vs 5.2%), insulin (10.6 vs 7.1 μIU/mL), homeostatic model assessment of insulin resistance (2.2 vs 1.7), total cholesterol (199 vs 171 mg/dL), and low-density lipoprotein cholesterol (123 vs 105 mg/dL), and lower triglyceride levels (74 vs 76 mg/dL). Significant 12-week GDM predictors included greater maternal weight gain (delta: 3.4 vs 1.5 kg) and higher levels of insulin (11.3 vs 7.6 μIU/mL), triglycerides (178 vs 120 mg/dL), and homeostatic model assessment of insulin resistance (2.3 vs 1.5). Twelve-week BMI is a predictor of GDM following adjustment for polycystic ovary syndrome status and maternal age. CONCLUSION: While preconception maternal BMI, age, and follicle-stimulating hormone/luteinizing hormone ratio are predictors of subsequent development of GDM, early IVF-conceived gestational weight gain is the best predictor of GDM onset.

[18] *Yagi R, Inoue K*. **Trends in Brand-name Statin Prescriptions Among Physicians Prescribing PCSK9 inhibitors in 2016-2018**. Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34126248
ABSTRACT

[19] *Deshpande M, Phadke M, Khan Abid T, Mahajan AU*. **A case report of successful complex percutaneous coronary intervention for acute coronary syndrome in a paediatric patient with familial hypercholesterolaemia**. European heart journal. Case reports 2021; 5:ytab175.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34142008
ABSTRACT
BACKGROUND: Familial hypercholesterolaemia (FH) is a primary genetic dyslipidaemia characterized by elevation in serum low-density lipoprotein cholesterol and its deposition in systemic arteries, which causes premature atherosclerosis. CASE SUMMARY: A 10-year-old girl presented with severe symptomatic coronary artery disease. She demonstrated characteristic morphological features of FH. Despite aggressive medical management and lipid-lowering therapy, her symptoms were not relieved and she had dynamic electrocardiogram changes. Coronary angiography showed a distal left main coronary artery lesion along with significant lesions in ostio-proximal and mid-left circumflex artery which were managed by provisional left main coronary artery to left circumflex artery

stenting technique, with good immediate- and short-term results and angina relief. DISCUSSION: To the best of our knowledge, this is the first reported case of a paediatric patient with FH and acute coronary syndrome treated with percutaneous coronary intervention to left main coronary artery and left circumflex artery using provisional stenting technique. Revascularization strategies for symptomatic coronary artery disease in paediatric patients with FH have multiple unique challenges and remain an unexplored and under-reported subject.

[20] *Sjuls S, Jensen U, Littmann K et al.* **Effective cholesterol lowering after myocardial infarction in patients with nephrotic syndrome may require a multi-pharmacological approach: a case report**. European heart journal. Case reports 2021; 5:ytab151.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34124564
ABSTRACT
BACKGROUND: Nephrotic syndrome causes severe hypercholesterolaemia due to increased production and altered clearance of lipoproteins from the liver. It is challenging for patients with nephrotic syndrome and coronary heart disease to meet LDL-cholesterol (LDL-C) goals for secondary prevention with conventional lipid-lowering therapy. CASE SUMMARY: We present a man with nephrotic syndrome caused by focal segmental glomerular sclerosis (FSGS) and hypercholesterolaemia. He presented at the emergency room (ER) with an ST-elevation myocardial infarction at the age of 26. On follow-up, the patient had persistent hypercholesterolaemia [LDL-C 3.9 mmol/L and lipoprotein(a) 308 nmol/L] despite a combination of lipid-lowering therapy with atorvastatin 80 mg/day and ezetimibe 10 mg/day. Addition of the proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitory antibody evolocumab 140 mg bi-monthly did not improve cholesterol levels. However, after addition of the sodium-glucose cotransporter 2 (SGLT2) inhibitor empagliflozin 10 mg/day on top of other anti-proteinuric treatments, the patient's proteinuria was reduced and a dramatic drop in LDL-C level by 3.2-0.6 mmol/L (-81%) was observed when evolocumab was re-introduced. DISCUSSION: We show that target LDL-C levels were obtained in this patient with therapy-resistant FSGS and hypercholesterolaemia following multi-pharmacological treatment with SGLT2 and PCSK9 inhibitors on top of conventional lipid-lowering therapy. The SGLT2-inhibitor reduced proteinuria and, speculatively, also reduced urinary loss of PCSK9-antibody. Therefore, in patients with nephrotic syndrome and cardiovascular disease novel therapeutic options to manage proteinuria could be considered to improve the efficacy of the lipid-lowering therapy, especially when the protein-based PCSK9 inhibitors are used.

[21] *Wang S, Wu T, Zuo Z et al.* **Comparison of cardiovascular outcomes and cardiometabolic risk factors between patients with type 2 diabetes treated with sodium-glucose cotransporter-2 inhibitors and dipeptidyl peptidase-4 inhibitors: a meta-analysis**. European journal of preventive cardiology 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34136913
ABSTRACT
AIMS : Prevention of cardiovascular outcomes is a goal of the management of patients with type 2 diabetes mellitus patients as important as lowering blood glucose levels. Among the various glucose-lowering agents, the effects of sodium-glucose cotransporter-2 inhibitors (SGLT-2Is) and dipeptidyl peptidase-4 inhibitors (DPP-4Is) on cardiovascular outcomes have become the focus of recent researches. METHODS AND RESULTS : A systematic search was performed through several

online database. All studies that compared the effects of SGLT-2Is and DPP-4Is on cardiovascular outcomes and cardiometabolic risk factors were reviewed. A total of 30 studies were included. Compared with DPP-4Is, SGLT-2Is treatment reduced the risk of stroke [risk ratio (RR) = 0.80; 95% confidence interval (CI), 0.76-0.84], myocardial infarction (RR = 0.85; 95% CI, 0.81-0.89), heart failure (RR = 0.58; 95% CI, 0.54-0.62), cardiovascular mortality (RR = 0.55; 95% CI, 0.51-0.60), and all-cause mortality (RR = 0.60; 95% CI, 0.57-0.63). In addition, SGLT-2Is presented favourable effects on hemoglobinA1c, fasting plasma glucose, systolic blood pressure, and diastolic blood pressure. The differences in blood lipids were also compared. CONCLUSION: Sodium-glucose cotransporter-2 inhibitors are superior to DPP-4Is in terms of cardiovascular outcomes. Sodium-glucose cotransporter-2 inhibitors bring more benefits with respect to the cardiometabolic risk factors.

[22] *Kim MJ, Kwak HS, Hwang SB, Chung GH*. **One-step evaluation of intraplaque hemorrhage in the carotid artery and vertebrobasilar artery using simultaneous non-contrast angiography and intraplaque hemorrhage**. European journal of radiology 2021; 141:109824.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34126430

ABSTRACT

PURPOSE: To investigate the one-step detection of intraplaque hemorrhage (IPH) in the carotid artery (CA) and vertebrobasilar artery (VBA) using simultaneous non-contrast angiography and intraplaque hemorrhage (SNAP). METHODS: From January 2019 to March 2020, 1820 consecutive patients who visited our emergency room for evaluation of neurologic symptoms underwent brain MR imaging, including the SNAP sequence. SNAP imaging examined the coronal section from the CA to the VBA. IPH was defined as plaque in the CA and VBA with 200 % higher signal intensity on SNAP than in adjacent muscle in at least two consecutive slices. RESULTS: Of these patients, 360 (19.8 %) had carotid plaque (both sides = 141, 39.2 %; single side = 219, 61.8 %). Of patients with carotid plaque, 185 (51.4 %) had IPH. Of 141 patients with plaques on both sides, 35 (24.8 %) had bilateral IPH. In total, 73 (4.0 %) patients had VBA IPH (30 with carotid plaque, 43 without carotid plaque). In addition, 18 (1.0 %) patients had carotid IPH and VBA IPH. Maximal wall thickness was significantly higher in the carotid IPH groups (4.5 ± 0.1 vs. 4.1 ± 0.1, $p = 0.009$). Prevalence of high grade stenosis (>70 %) was significantly higher in the carotid IPH group (17.5 % vs. 6.2 %, $p < 0.001$). CONCLUSIONS: SNAP imaging can be evaluated with a one-step examination of CA and VBA IPH.

[23] *Zhang H, Jiang M, Hou H, Li Q*. **Efficacy of simvastatin on carotid atherosclerotic plaque and its effects on serum inflammatory factors and cardiocerebrovascular events in elderly patients**. Experimental and therapeutic medicine 2021; 22:819.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34131442

ABSTRACT

To investigate the efficacy of simvastatin on carotid atherosclerotic plaque (CAP) and its effects on serum inflammatory factors and cardiocerebrovascular events in elderly patients, 130 elderly patients with CAP were randomly divided into observation (n=65) and control groups (n=65). The control group was treated with 75 mg/day aspirin enteric-coated tablets, and the observation group was administered additional 20 mg/day simvastatin. Serum total cholesterol, triglyceride, and high- and low-density lipoprotein cholesterol levels (evaluated via the endpoint method) were determined in both groups. Furthermore, the length, thickness and number of CAPs was measured using color Doppler ultrasonography. In addition, levels of inflammatory biomarkers including high-sensitivity C-

reactive protein (hs-CRP), tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), nitric oxide, D-dimer and fibrinogen, as well as change in microemboli count, were also compared After treatment, the observation group exhibited a significant reduction in size, thickness, and number of CAP and intima-media thickness compared with before treatment. However, no significant difference was found in the indicators of CAPs in the control group before and after treatment. The levels of total cholesterol, triglyceride, and low-density lipid cholesterol decreased, while high-density lipid cholesterol increased in the observation group after treatment, with notable changes in the observation group compared with in the control group. Overall response rate was higher in the observation group compared with the control group. TNF-α, IL-6, and hs-CRP levels in the observation group decreased after treatment compared with those before treatment and those in the control group. Furthermore, the rate of microemboli positivity was lower in the observation group than in the control group. Moreover, the overall incidence of acute cardiocerebrovascular events was lower in the observation group than in the control group. Therefore, it was demonstrated that simvastatin can reduce blood lipid levels, decrease the quantity and size of plaques, alleviate inflammatory response, reduce microemboli formation and reduce the risk of cardiocerebrovascular events in elderly patients with CAP.

[24] *Khan MY, Pandit S, Guha S et al.* **Demographic profile, clinical characteristics and medical management patterns of Indian coronary artery disease patients: a nationwide urban-based, real-world, retrospective, observational electronic medical record study- report of baseline data**. Expert review of cardiovascular therapy 2021:1-7.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34126829
ABSTRACT
Background: This is the first detailed Indian electronic medical record (EMR)-based real-world observational study to understand the clinical characteristics, associated comorbidities/risk factors and treatment(s) of CAD patients across India.Methods: EMR data of adult Indians (aged ≥ 18 years) diagnosed with CAD was retrospectively analyzed.Results: The majority of the participants had stable IHD (93%), were men (68.5% in ACS, 59.8% in stable IHD), most common age group was 40-64 years in ACS (56.6%) and stable IHD (51.4%). Both are common in metros (ACS 52%, 62% stable IHD). There is a high frequency of hypertension (38.2% in ACS, 59% in stable IHD) and diabetes mellitus (32.3% in ACS, 57.6% in stable IHD). Most common treatments are antiplatelet drugs and lipid-lowering drugs (96%).Conclusions: In India, stable IHD is the most prevalent form in vast majority of patients. The patients with CAD are mostly males, are mainly located in metros and majority fall between the age group of 40-64. The major comorbidities are hypertension and diabetes mellitus. Sociodemographic and clinical characteristics for CAD in India may not be similar to what is reported from the west. There is a significant difference in drug usage and adherence to guidelines in India for CAD.

[25] **Bezafibrate Add-On Therapy Improves Liver Transplantation-Free Survival in Patients With Primary Biliary Cholangitis: A Japanese Nationwide Cohort Study**. Gastroenterol Hepatol (N Y) 2021; 17:10-11.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34135715
ABSTRACT

[26] *Ma X, Liu Z, Ilyas I et al.* **GLP-1 receptor agonists (GLP-1RAs): cardiovascular actions and therapeutic potential**. International journal of biological sciences 2021; 17:2050-2068.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34131405

ABSTRACT

Type 2 diabetes mellitus (T2DM) is closely associated with cardiovascular diseases (CVD), including atherosclerosis, hypertension and heart failure. Some anti-diabetic medications are linked with an increased risk of weight gain or hypoglycemia which may reduce the efficacy of the intended anti-hyperglycemic effects of these therapies. The recently developed receptor agonists for glucagon-like peptide-1 (GLP-1RAs), stimulate insulin secretion and reduce glycated hemoglobin levels without having side effects such as weight gain and hypoglycemia. In addition, GLP1-RAs demonstrate numerous cardiovascular protective effects in subjects with or without diabetes. There have been several cardiovascular outcomes trials (CVOTs) involving GLP-1RAs, which have supported the overall cardiovascular benefits of these drugs. GLP1-RAs lower plasma lipid levels and lower blood pressure (BP), both of which contribute to a reduction of atherosclerosis and reduced CVD. GLP-1R is expressed in multiple cardiovascular cell types such as monocyte/macrophages, smooth muscle cells, endothelial cells, and cardiomyocytes. Recent studies have indicated that the protective properties against endothelial dysfunction, anti-inflammatory effects on macrophages and the anti-proliferative action on smooth muscle cells may contribute to atheroprotection through GLP-1R signaling. In the present review, we describe the cardiovascular effects and underlying molecular mechanisms of action of GLP-1RAs in CVOTs, animal models and cultured cells, and address how these findings have transformed our understanding of the pharmacotherapy of T2DM and the prevention of CVD.

[27] *Hess CN, Cannon CP, Beckman JA et al.* **Effectiveness of Blood Lipid Management in Patients With Peripheral Artery Disease**. Journal of the American College of Cardiology 2021; 77:3016-3027.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34140105

ABSTRACT

BACKGROUND: Low-density lipoprotein cholesterol (LDL-C) is associated with heightened risk of major adverse cardiovascular events (MACE) and major adverse limb events (MALE) in peripheral artery disease (PAD). Lipid-lowering therapies (LLT) that reduce LDL-C decrease this risk. OBJECTIVES: The authors examined LLT use and actual achieved LDL-C in PAD. METHODS: PAD patients in MarketScan from 2014 to 2018 were identified. Outcomes included LLT use, defined as high-intensity (HI) (high-intensity statin, statin plus ezetimibe, or PCSK9 inhibitor), low-intensity (any other lipid regimen), or no therapy, and follow-up LDL-C. Factors associated with LDL-C <70 mg/dl were identified with multivariable logistic regression. RESULTS: Among 250,103 PAD patients, 20.5% and 39.5% were treated at baseline with HI and low-intensity LLT, respectively; 40.0% were on no LLT. Over a 15-month median follow-up period, HI LLT use increased by 1.5%. Among 18,747 patients with LDL-C data, at baseline, 25.1% were on HI LLT, median LDL-C was 91 mg/dl, and 24.5% had LDL-C <70 mg/dl. Within the HI LLT subgroup, median LDL-C was 81 mg/dl, and 64% had LDL-C ≥70 mg/dl. At follow-up, HI LLT use increased by 3.7%, median LDL-C decreased by 4.0 mg/dl, and an additional 4.1% of patients had LDL-C <70 mg/dl. HI LLT use was greater after follow-up MACE (55.0%) or MALE (41.0%) versus no ischemic event (26.1%). After MACE or MALE, LDL-C was <70 mg/dl in 41.5% and 36.1% of patients, respectively, versus 27.1% in those without an

event. Factors associated with follow-up LDL-C <70 mg/dl included smoking, hypertension, diabetes, prior lower extremity revascularization, and prior myocardial infarction but not prior acute or critical limb ischemia. CONCLUSIONS: In PAD, LLT use is suboptimal, LDL-C remains elevated, and LLT intensity is a poor surrogate for achieved LDL-C. Less aggressive lipid management was observed in PAD versus cardiovascular disease, highlighting missed opportunities for implementation of proven therapies in PAD.

[28] *Secemsky EA, Carroll BJ, Krawisz AK*. **The Ongoing Struggle to Optimize Lipid-Lowering Therapy in Patients With PAD: PADdling in Circles**. Journal of the American College of Cardiology 2021; 77:3028-3030.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34140106
ABSTRACT

[29] *Tao L, Chen HS*. **Reply: Imaging of Vulnerable Intracranial Atherosclerotic Plaque for Embolic Stroke of Undetermined Source**. Journal of the American College of Cardiology 2021; 77:3140-3141.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34140115
ABSTRACT

[30] *Zhu C, Malhotra A, Mossa-Basha M*. **Imaging of Vulnerable Intracranial Atherosclerotic Plaque for Embolic Stroke of Undetermined Source**. Journal of the American College of Cardiology 2021; 77:3140.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34140114
ABSTRACT

[31] *Bonano JC, Aratani AK, Sambare TD et al.* **Perioperative Statin Use May Reduce Postoperative Arrhythmia Rates After Total Joint Arthroplasty**. The Journal of arthroplasty 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34127349
ABSTRACT
BACKGROUND: Postoperative arrhythmias are associated with increased morbidity and mortality in total joint arthroplasty (TJA) patients. HMG-CoA (3-hydroxy-3-methyl-glutaryl-CoA) reductase inhibitors (statins) decrease atrial fibrillation rates after cardiac surgery, but it is unknown if this cardioprotective effect is maintained after joint reconstruction surgery. We aim to determine if perioperative statin use decreases the incidence of 90-day postoperative arrhythmias in patients undergoing primary TJA. METHODS: We performed a single-center retrospective cohort study in which 231 primary TJA patients (109 hips, 122 knees) received simvastatin 80 mg daily during their hospitalization as part of a single surgeon's standard postoperative protocol. This cohort was matched to 966 primary TJA patients (387 hips and 579 knees) that did not receive simvastatin. New-onset arrhythmias (bradycardia, atrial fibrillation/tachycardia/flutter, paroxysmal supraventricular tachycardia, and ventricular tachycardia) and complications (readmissions, thromboembolism, infection, and dislocation) within 90 days of the procedure were documented. Categorical variables were analyzed using Fisher's exact tests. Our study was powered to detect a 3% difference in arrhythmia rates. RESULTS: Within 90 days postoperatively, arrhythmias occurred in 1 patient (0.4%) who received a perioperative statin, 39 patients (4.0%) who did not receive statins (P = .003), and 24

patients (4.2%) who were on outpatient statins (P = .005). This is 10-fold reduction in the relative risk of developing a postoperative arrhythmia within 90 days of arthroplasty and an absolute risk reduction of 3.6%. CONCLUSION: Treating as few as 28 patients with perioperative simvastatin prevents one new cardiac arrhythmia within 90 days in statin-naïve patients undergoing TJA.

[32] *Zhou R, Stouffer GA, Smith SC, Jr.* **Targeting the Cholesterol Paradigm in the Risk Reduction for Atherosclerotic Cardiovascular Disease: Does the Mechanism of Action of Pharmacotherapy Matter for Clinical Outcomes?** Journal of cardiovascular pharmacology and therapeutics 2021:10742484211023632.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34138676
ABSTRACT
Hypercholesterolemia is a well-established risk factor for atherosclerotic cardiovascular disease (ASCVD). Low-density lipoprotein cholesterol (LDL-C) has been labeled as "bad" cholesterol and high-density lipoprotein cholesterol (HDL-C) as "good" cholesterol. The prevailing hypothesis is that lowering blood cholesterol levels, especially LDL-C, reduces vascular deposition and retention of cholesterol or apolipoprotein B (apoB)-containing lipoproteins which are atherogenic. We review herein the clinical trial data on different pharmacological approaches to lowering blood cholesterol and propose that the mechanism of action of cholesterol lowering, as well as the amplitude of cholesterol reduction, are critically important in leading to improved clinical outcomes in ASCVD. The effects of bile acid sequestrants, fibrates, niacin, cholesteryl ester transfer protein (CETP) inhibitors, apolipoprotein A-I and HDL mimetics, apoB regulators, acyl coenzyme A: cholesterol acyltransferase (ACAT) inhibitors, cholesterol absorption inhibitors, statins, and proprotein convertase subtilisin kexin 9 (PCSK9) inhibitors, among other strategies are reviewed. Clinical evidence supports that different classes of cholesterol lowering or lipoprotein regulating approaches yielded variable effects on ASCVD outcomes, especially in cardiovascular and all-cause mortality. Statins are the most widely used cholesterol lowering agents and have the best proven cardiovascular event and survival benefits. Manipulating cholesterol levels by specific targeting of apoproteins or lipoproteins has not yielded clinical benefit. Understanding why lowering LDL-C by different approaches varies in clinical outcomes of ASCVD, especially in survival benefit, may shed further light on our evolving understanding of how cholesterol and its carrier lipoproteins are involved in ASCVD and aid in developing effective pharmacological strategies to improve the clinical outcomes of ASCVD.

[33] *Roberts R, Fair J.* **A Less than Provocative Approach for the Primary Prevention of CAD**. Journal of cardiovascular translational research 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34128181
ABSTRACT
Coronary artery disease (CAD) risk increases in proportion to the magnitude and duration of exposure to plasma low-density lipoprotein cholesterol (LDL-C), doubling every additional decade of exposure. Early primary prevention is three times more effective than initiated later. Several clinical trials show plasma LDL-C of 15-40 mg/dL is more effective and equally safe as the Current Cardiovascular Clinical Practice Guidelines (CCCPG) recommended target of 70mg/dL. The cholesterol in the blood is the excess synthesized by the cells and secreted into the blood for disposal in the liver. The CCCPG is inadequate since traditional risk factors (TRF) are not detectable until the sixth and seventh decade. The genetic risk score (GRS) evaluated in 1 million individuals as a risk

stratifier for CAD is superior to TRF. Genetic risk for CAD was reduced by 30-50% by statin therapy, PCSK9 inhibitors, and lifestyle changes. The GRS does not change during one's lifetime and is inexpensive. Incorporating genetic risk stratification into CCCPG would induce a paradigm shift in the primary prevention of CAD.

[34] *Fanous MM, Gianos E, Sperling LS et al.* **Early use of PCSK9 inhibitor therapy after heart transplantation from a hepatitis C virus positive donor**. Journal of clinical lipidology 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34120877

ABSTRACT

Although statin therapy is a primary treatment to prevent cardiac allograft vasculopathy (CAV), its use may be delayed due to pharmacologic interactions in the early post-transplant period among heart transplant (HT) recipients with hepatitis C virus positive (HCV+) donors. Further examination of the possible benefits of early, nonstatin lipid-lowering therapies (LLT), such as PCSK9 inhibitors (PCSK9i), among this specific subset of transplant recipients is therefore becoming increasingly important. We report a 60-year-old man who received a HT from a HCV+ donor for end-stage ischemic cardiomyopathy. In the early post-transplant period, there was concern for drug-drug interactions between statin, immunosuppressant, and direct acting antiviral (DAA) therapy. In addition, prior to transplant, he reported statin-associated muscle symptoms in response to multiple statins, which persisted despite attempts to re-challenge and use an every-other-day dosing strategy. Therefore, the patient was started on PCSK9i therapy after transplantation and while receiving curative DAA therapy for HCV. As the number of HT recipients of HCV+ donors continue to rise, investigation into the safety and benefits of early use of PCSK9i for the reduction of CAV and improved cardiovascular and mortality outcomes should be pursued.

[35] *Maher LL, Tokgözoğlu SL, Sanchez EJ et al.* **JCL Roundtable: Global Think Tank on Lipoprotein(a)**. Journal of clinical lipidology 2021; 15:387-393.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34144765

ABSTRACT

Lipoprotein(a) operates in causal pathways to promote atherosclerosis, arterial thrombosis, and aortic stenosis. It has been associated with rare cases of nonatherosclerotic arterial thrombotic stroke at any age. Inherited variation of lipoprotein(a) levels substantially increases cardiovascular risk in 20% of people worldwide. Recent progress in identifying the risk associated with lipoprotein(a) and in pursuing effective treatment has led to a recent Global Think Tank including representatives from the European Atherosclerosis Society, American Heart Association, Preventive Cardiovascular Nurses Association, National Lipid Association, and other groups. The need for standardized laboratory measurement in nanomoles per liter met with unanimous consensus. Atherosclerotic risk is linearly associated with plasma lipoprotein(a) levels, so that persons with the highest levels may have risk similar to other severe inherited lipoprotein disorders. Universal once-in-lifetime screening has been recommended by European and Canadian cardiovascular societies, but not by U.S. organizations. Current pharmacologic therapies are limited to 20-30% lowering of lipoprotein(a) levels, and no pharmacologic treatment for lowering lipoprotein(a) has yet been proven to reduce risk in a cardiovascular outcomes trial. Treatment for high-risk patients focuses on reducing low density lipoprotein cholesterol and other risk factors. New therapies targeting messenger RNA for apolipoprotein(a) can achieve 80-90% reduction of lipoprotein(a) levels. One such therapy using a

liver-directed antisense oligonucleotide is currently being tested in a large cardiovascular outcomes trial. Increased recognition of lipoprotein(a)-associated risk and emergence of potentially effective therapy together lead to a mandate for a unified global effort on education, standardization, and clinical management.

[36] *Schaefer EJ, Tint GS, Duell PB, Steiner RD*. **Cerebrotendinous xanthomatosis, sitosterolemia, Smith-Lemli-Opitz syndrome and the seminal contributions of Gerald Salen, MD (1935-2020)**. Journal of clinical lipidology 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34140251
ABSTRACT
Cerebrotendinous xanthomatosis (CTX), sitosterolemia, and Smith-Lemli Opitz syndrome (SLOS) are rare inborn errors of metabolism. The diagnoses of CTX and sitosterolemia are often delayed for many years because of lack of physician awareness, often resulting in significant and unnecessary progression of disease. CTX may present with chronic diarrhea, juvenile onset cataracts, strikingly large xanthomas, and neurologic disease in the setting of a normal serum cholesterol, but markedly elevated serum or plasma cholestanol levels. These patients have a defect in producing the bile acid chenodoxycholate, and oral chenodeoxycholate therapy is essential for these patients in order to prevent neurologic complications. Sitosterolemia can present with xanthomas, anemia, thrombocytopenia, splenomegaly, very premature heart disease, and serum cholesterol levels that may be normal or elevated, along with marked elevations of plasma β-sitosterol. These patients have a defect causing overabsorption of β-sitosterol, and the treatment of choice is oral ezetimibe. SLOS presents with growth delay, intellectual disability, multiple structural anomalies, and low serum cholesterol levels, and the defect is reduced cholesterol production. Treatment consists of dietary cholesterol supplementation and oral bile acid therapy which raises serum cholesterol levels and may improve symptoms. The metabolic and genetic defects in these disorders have been defined. There is no one in our field that has contributed more to the diagnosis and treatment of these disorders than Gerald Salen, MD, who died in late 2020 at 85 years of age. He will be greatly missed by his family, friends, and colleagues from around the world.

[37] *Basarir G, Ozcabi B, Aksu Sayman O et al.* **Evaluation of clinical, endocrine and metabolic findings in obese children with and without hepatosteatosis**. J Pediatr Endocrinol Metab 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34142516
ABSTRACT
OBJECTIVES: Non-alcoholic fatty liver disease (NAFLD) is a common obesity-related comorbidity in childhood. In this study, we aimed to evaluate predictors of NAFLD by comparing clinical, endocrine and metabolic findings in obese children with and without hepatosteatosis. METHODS: Two hundred and eight obese children aged 6-18 years were included. The patients were divided into group 1 (patients with NAFLD, n=94) and group 2 (patients without NAFLD, n=114). Anthropometric measurements, pubertal stage, lipid profiles, fasting glucose and insulin, homeostatic model of assessment for insulin resistance (HOMA-IR), uric acid, total bilirubin, alanine aminotransferase (ALT), blood urea nitrogen, thyroid-stimulating hormone and free thyroxine parameters were compared retrospectively. RESULTS: The mean body weight, body mass index (BMI), height, tri-ponderal mass index (TMI), insulin, HOMA-IR, triglyceride, ALT and uric acid values were significantly higher, while high-density lipoprotein-cholesterol (HDL-C) values were significantly lower in group 1.

The 70.7% of obese children with hepatosteatosis and 83.9% of those without hepatosteatosis were correctly estimated by parameters including age, gender, ALT, HDL-C, fasting insulin and uric acid values. CONCLUSIONS: Since obesity-associated hepatosteatosis induces various long-term metabolic impacts in children, early detection is of critical importance. Age, gender, TMI, BMI, ALT, HDL-C, fasting insulin and uric acid values may help to predict the risk of hepatosteatosis. Besides, we assessed whether TMI compared to BMI does not have a better utility in estimating obesity-induced hepatosteatosis in children. This is the first study to show the association between TMI and hepatosteatosis in children.

[38] *Cannon CP, de Lemos JA, Rosenson RS et al.* **Use of Lipid-Lowering Therapies Over 2 Years in GOULD, a Registry of Patients With Atherosclerotic Cardiovascular Disease in the US**. JAMA cardiology 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34132735

ABSTRACT

IMPORTANCE: Guidelines for patients with atherosclerotic cardiovascular disease (ASCVD) recommend intensive statin therapy and adding nonstatin therapy if low-density lipoprotein cholesterol (LDL-C) levels are 70 mg/dL or more. Compliance with guidelines is often low. OBJECTIVE: To track LDL-C treatment patterns in the US over 2 years. DESIGN, SETTING, AND PARTICIPANTS: GOULD is a prospective observational registry study involving multiple centers. Patients with ASCVD receiving any lipid-lowering therapy (LLT) were eligible. Between December 2016 and July 2018, patients were enrolled in 1 of 3 cohorts: (1) those currently receiving proprotein convertase subtilisin/kexin type 9 inhibitor (PCSK9i) and 2 groups not receiving PCSK9i drugs, with (2) LDL-C levels of 100 mg/dL or more or (3) LDL-C levels of 70 to 99 mg/dL. Patients had medical record reviews and telephone interviews every 6 months. Analysis was done on data collected as of October 5, 2020. MAIN OUTCOMES AND MEASURES: The primary outcome was the change in LLT use in 2 years. Secondary outcomes included the number of LDL-C measurements, LDL-C levels, and responses to structured physician and patient questionnaires over 2 years. RESULTS: A total of 5006 patients were enrolled (mean [SD] age, 67.8 [9.9] years; 1985 women [39.7%]; 4312 White individuals [86.1%]). At 2 years, 885 (17.1%) had LLT intensification. In the cohorts with LDL-C levels of 100 mg/dL or more and 70 to 99 mg/dL, LLT intensification occurred in 403 (22.4%) and 383 (14.4%), respectively; statins were intensified in 115 (6.4%) and 168 (6.3%), ezetimibe added in 123 (6.8%) and 118 (4.5%), and PCSK9i added in 114 (6.3%) and 58 (2.2%), respectively. In the PCSK9i cohort, 508 of 554 (91.7%) were still taking PCSK9i at 2 years. Lipid panels were measured at least once over 2 years in 3768 patients (88.5%; PCSK9i cohort, 492 [96.1%]; LDL-C levels ≥100 mg/dL or more, 1294 [85.9%]; 70-99 mg/dL, 1982 [88.6%]). Levels of LDL-C fell from medians (interquartile ranges) of 120 (108-141) mg/dL to 95 (73-118) mg/dL in the cohort with LDL-C levels of 100 mg/dL or more, 82 (75-89) to 77 (65-90) mg/dL in the cohort with LDL-C levels of 70 to 99 mg/dL, and 67 (42-104) mg/dL to 67 (42-96) mg/dL in the PCSK9i cohort. Levels of LDL-C less than 70 mg/dL at 2 years were achieved by 308 patients (21.0%) and 758 patients (33.9%) in the cohorts with LDL-C levels of 100 mg/dL or more and 70 to 99 mg/dL, respectively, and 272 patients (52.4%) in the PCSK9i cohort. At 2 years, practice characteristics were associated with more LLT intensification (teaching vs nonteaching hospitals, 148 of 589 [25.1%] vs 600 of 3607 [16.6%]; lipid protocols or none, 359 of 1612 [22.3%] vs 389 of 2584 [15.1%]; cardiology, 452 of 2087 [21.7%] vs internal or family medicine, 204 of 1745 [11.7%] and other, 92 of 364 [25.3%]; all $P < .001$) and achievement of LDL-C less than

70 mg/dL (teaching vs nonteaching hospitals, 173 of 488 [35.5%] vs 823 of 2986 [27.6%]; lipid protocols vs none, 451 of 1411 [32.0%] vs 545 of 2063 [26.4%]; both P < .001; cardiology, 523 of 1686 [30.1%] vs internal or family medicine, 377 of 1472 [25.6%] and other, 96 of 316 [30.4%]; P = .003). CONCLUSIONS AND RELEVANCE: Of patients with ASCVD, most with suboptimal LDL-C levels at baseline, only 17.1% had LLT intensification after 2 years, and two-thirds remained at an LDL-C level greater than 70 mg/dL. Further intensive efforts are needed to achieve optimal LDL-C management in patients with ASCVD.

[39] *Skowroński J, Mintz GS, Michałowska I et al.* **Impact of diabetes mellitus on the dimensions of normal atherosclerosis-free coronary arteries**. Kardiol Pol 2021; 79:566-568.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34125931
ABSTRACT

[40] *Sen A*. **Does serotonin deficiency lead to anosmia, ageusia, dysfunctional chemesthesis and increased severity of illness in COVID-19?** Medical hypotheses 2021; 153:110627.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34139598
ABSTRACT
Different mechanisms forwarded to understand anosmia and ageusia in coronavirus patients are not adequate to explain reversible anosmia and ageusia, which are resolved quickly. In addition, the reason behind the impaired chemesthetic sensations in some coronavirus patients remains unknown. In the present paper it is proposed that SARS-CoV-2 patients suffer from depletion of tryptophan, as ACE2, a key element in the process of absorption of tryptophan from the food, is significantly reduced in the patients as coronavirus uses ACE2 as the receptor to enter the host cells. The tryptophan depletion leads to a deficit of serotonin (5-HT) in SARS-COV-2 patients because tryptophan is the precursor in the synthesis of 5-HT. Such 5-HT deficiency can explain anosmia, ageusia and dysfunctional chemesthesis in COVID-19, given the fact that 5-HT is an important neuromodulator in the olfactory neurons, taste receptor cells and transient receptor potential channels (TRP channels) involved in chemesthesis. In addition, 5-HT deficiency worsens silent hypoxemia and depresses hypoxic pulmonary vasoconstriction leading to increased severity of the disease. Also, the levels of anti-inflammatory melatonin (synthesized from 5-HT) and nicotinamide adenine dinucleotide (NAD(+), produced from niacin whose precursor is the tryptophan) might decrease in coronavirus patients resulting in the aggravation of the disease. Interestingly, selective serotonin reuptake inhibitors (SSRIs) may not be of much help in correcting the 5-HT deficiency in COVID-19 patients, as their efficacy goes down significantly when there is depletion of tryptophan in the system. Hence, tryptophan supplementation may herald a radical change in the treatment of COVID-19 and accordingly, clinical trials (therapeutic / prophylactic) should be conducted on coronavirus patients to find out how tryptophan supplementation (oral or parenteral, the latter in severe cases where there is hardly any absorption of tryptophan from the food) helps in curing, relieving or preventing the olfactory, gustatory and chemesthetic dysfunctions and in lessening the severity of the disease.

[41] *Chen LL, Zheng JH*. **Effects of atorvastatin on the insulin resistance in women of polycystic ovary syndrome: A systematic review and meta-analysis**. Medicine (Baltimore) 2021; 100:e26289.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34128863

ABSTRACT
BACKGROUND: Atorvastatin treatment has been suggested as a therapeutic method for women with polycystic ovary syndrome (PCOS) in many clinical studies. Nonetheless, the effects of atorvastatin on insulin resistance in PCOS patients still remain controversial. OBJECTIVE: The aim of this report was to evaluate the effects of atorvastatin therapy on the insulin resistance in the treatment of PCOS compared to that of placebo, in order to confer a reference for clinical practice. METHODS: Randomized controlled trials (RCTs) of atorvastatin for PCOS published up to August, 2020 were searched. Standardized mean difference (SMD) and 95% confidence interval (CI) were calculated, and heterogeneity was measured by the I2 test. Sensitivity analysis was also carried out. The outcomes of interest were as follows: fasting glucose concentration, fasting insulin level, homeostasis model assessment of insulin resistance (HOMA-IR) or body mass index (BMI) value. RESULTS: Nine RCTs with 406 participants were included. The difference of fasting glucose concentration in PCOS patients between atorvastatin group and placebo group was not statistically significant (8 trials; SMD -0.06, 95% CI -0.31 to 0.20, P=.66). PCOS patients in atorvastatin group had lower fasting insulin level than those in placebo group (7 trials; SMD -1.84, 95% CI -3.06 to -0.62, P<.003). The homeostasis model assessment of insulin resistance (HOMA-IR) value showed significant decrease in the atorvastatin therapy compared to placebo (6 trials; SMD -4.12, 95% CI -6.00 to -2.23, P<.0001). In contrast to placebo, atorvastatin therapy did not decrease the BMI value significantly in PCOS patients (7 trials; SMD 0.12, 95% CI -0.07 to 0.31, P=.22). CONCLUSIONS: Atorvastatin therapy can reduce insulin resistance in the treatment of patients with PCOS. In addition, further large-sample, multi-center RCTs are needed to identify these findings.

[42] *Li K, Liu MM, Yang X et al.* **Evaluation of efficacy and safety of combined rosuvastatin and atorvastatin in treating with coronary heart disease: A protocol for systematic review and meta-analysis**. Medicine (Baltimore) 2021; 100:e26340.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34128881

ABSTRACT
BACKGROUND: Globally, coronary heart disease (CHD) is a primary cause of morbidity leading to disabilities and mortality. Modern clinical practice adopts several pharmacological methods to treat CHD. Angina pectoris refers to sever chest pain due to CHD, it has a profound impact on the wellbeing of patients. Moreover, angina pectoris is a crucial prognosis predictor. The aim of the current study is to evaluate the effectiveness and safeness of using combined rosuvastatin and atorvastatin to treat CHD patients. METHODS: A systematic literature search for articles will be conducted on several electronic databases from their inception to May 2021. The search will include all randomized controlled trials examining the use of rosuvastatin in combination with atorvastatin to treat CHD patients. The databases are as follows: MEDLINE, Web of Science, the Cochrane Library, WanFang database, China National Knowledge Infrastructure, and EMBASE. A couple of authors will independently assess the eligibility, extract study data, and assess the possibility of bias. Moreover, depending on the type of data and heterogeneity of the included studies, either the Mantel-Haensel fixed-effect model or the DerSimonian-Laird random-effect model will be used to estimate the relative risk, mean differences, or standardized mean differences and 95% confidence intervals. All differences in opinion shall be decided by involving an additional author in the discussion. Lastly, the RevMan software (version: 5.3) will be used to perform sensitivity analysis, data synthesis, and risk of bias assessment. RESULTS: The effectiveness and security of using rosuvastatin in combination with

atorvastatin to treat CHD patients will be systematically evaluated. CONCLUSION: This study will provide evidence to evaluate the efficacy and security of using a combination of rosuvastatin and atorvastatin to treat CHD patients. ETHICS AND DISSEMINATION: Ethical approval will not be required since it is based on already published data. REGISTRATION NUMBER: DOI 10.17605/OSF.IO/VYBDR (https://osf.io/vybdr/).

[43] *Xu Y, Zhang B, Chen Y et al.* **Simvastatin increases circulating endothelial progenitor cells and inhibits the formation of intracranial aneurysms in rats with diet-induced hyperhomocysteinemia**. Neurosci Lett 2021; 760:136072.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34147541
ABSTRACT
BACKGROUND AND PURPOSE: Endothelial dysfunction triggers early pathological changes in artery, leading to the formation of intracranial aneurysm (ICA). Increase in plasma homocysteine (Hcy) impairs endothelium and endothelial progenitor cells (EPCs) are critical in repairing damaged endothelium. The aim of this study was to assess the impact of simvastatin on ICA formation in rats with hyperhomocysteinemia (HHcy). METHODS: ICAs were induced in Male Sprague-Dawley rats after surgical induction in the presence of HHcy induced by a high L-methionine diet with or without oral simvastatin treatment. The size and media thickness of ICAs were evaluated 2 months after aneurysm induction. EPCs and serum vascular endothelial grow factor (VEGF) were measured be flow cytometry and ELISA respectively. Plasma Hcy levels and expression of VEGF, endothelial nitric oxide synthase (eNOS), inducible nitric oxide synthase (iNOS), matrix metalloproteinase-2 (MMP-2), and MMP-9 in aneurysmal walls were examined and correlated with ICA formation. RESULTS: HHcy accelerates ICA formation and rats treated with simvastatin exhibited a significant increase in media thickness and a reduction in aneurysmal size. Simvastatin increased levels of circulating EPCs and decreased iNOS, MMP-2, MMP-9 and VEGF mRNA levels, while increased eNOS mRNA in aneurysmal tissue. CONCLUSION: In a rat model, HHcy reduces circulating EPCs and accelerates ICA formation. Simvastatin treatment increases circulating EPCs and inhabits the formation of ICA. We have shown a close association among circulating EPCs, biochemical markers related to vascular remodeling and the formation of ICA.

[44] *Loss LC, Benini D, de Lima ESFX et al.* **Effects of omega-3 supplementation on muscle damage after resistance exercise in young women: a randomized placebo-controlled trial**. Nutrition and health 2021:2601060211022266.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34130550
ABSTRACT
BACKGROUND: Omega-3 is a nutritional strategie that have been used to recover muscles from exercise-induced muscle damage in a preventive perspective. AIM: To verify whether omega-3 (ω-3) supplementation after a session of resistance exercise facilitates muscle recovery in women undergoing a balanced diet. METHODS: This clinical trial was registered under the number NCT02839525. Thirty healthy women (22.2 ± 3.3 years) participated in this double-blinded, placebo-controlled trial. They were randomly distributed into ω-3 (n=15) and placebo (n=15) groups. They ingested ω-3 fish oil (3200 mg/day) or placebo (olive oil) at the dinner after the exercise bout (10 sets of 10 unilateral eccentric contractions in a knee extension chair), as well as at lunch for the three subsequent days. In addition, both groups followed a balanced diet along the four days. Muscle

soreness and maximal isometric and isokinetic voluntary contractions were assessed immediately before, and 24, 48, and 72 hours after the resistance exercise. MAIN FINDINGS: There was no significant group-time interaction for any outcome. Participants presented increased levels of muscle soreness and reduced muscle strength capacity along the three days after exercise. There was no difference between placebo and ω-3 groups. CONCLUSION: Supplementation of ω-3 fish oil for three days after resistance exercise provided no additional benefits compared to placebo supplementation on recovery of healthy young women following a balanced diet.

[45] *Paknahad Z, Moosavian SP, Mahdavi R, Rajabi P*. **The effects of olive oil and cholesterol enriched diets on aortic fatty streak development and lipid peroxidation in rabbits**. Nutrition and health 2021:2601060211022260.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34139909
ABSTRACT
BACKGROUND AND AIM: High plasma cholesterol levels, mainly low-density lipoprotein-cholesterol (LDL) is a widely recognized major risk factor for coronary heart disease (CHD). According to epidemiologic studies' findings, people from the Mediterranean countries have lower CHD rates than other countries; in these countries the usual diet is high in olive oil. The present study compares the effects of a cholesterol-enriched diet with or without adding olive oil on serum lipoproteins, lipid peroxidation, and atherosclerosis development. METHODS: Twenty Dutch male rabbits were categorized into four groups (one group as control, and others as experimental). They received one of control (CON), olive oil-rich (OIL), cholesterol-rich (CHOL), and cholesterol + olive oil (COIL) diet for 12 weeks. Fasting blood samples from the heart were collected at the beginning and the end of the experimental period. RESULTS: Means of serum lipids were not significantly different at the beginning of the experimental period. After the intervention, significant differences were shown in total cholesterol (TC) (CON: 27.75 ± 4.83, OIL: 19.75 ± 2.62, CHOL: 1757.20 ± 149.62, COIL: 2906.40 ± 421.01; $P < 0.001$), high-density lipoprotein-cholesterol (HDL-C) (CON: 16 ± 1.47, OIL: 10.25 ± 1.70, CHOL: 22.2 ± 3.83, COIL: 28.60 ± 6.27; $P = 0.04$), triglyceride (CON: 65 ± 12.21, OIL: 71.75 ± 6.23, CHOL: 244.2 ± 44.45, COIL: 775.6 ± 105.07; $P < 0.001$), and MDA between groups (CON: 0.57 ± 0.10, OIL: 0.63 ± 0.15, CHOL: 5.62 ± 0.18, COIL: 2.06 ± 0.64; $P < 0.001$). The comparison of CHOL and the COIL groups showed a higher mean of malondialdehyde (MDA) in group CHOL (4.47 ± 0.28 vs 1.1 ± 0.6; $P < 0.001$). Aortic lesion was not observed in CON and OIL groups. Aortic lesion degree was significantly lower in the COIL group compared to the CHOL (2.4 ± 0.6 vs 3.66 ± 0.33; $P = 0.02$). CONCLUSIONS: These findings showed the preventive effect of olive oil on atherosclerosis development. However, it is independent of the plasma lipoprotein effect, and olive oil probably acts on arteries directly.

[46] *Mok J, Malpartida JC, O'Dell K et al.* **Vascular comorbidities worsen prognosis of patients with heart failure hospitalised with COVID-19**. Open heart 2021; 8.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34127532
ABSTRACT
BACKGROUND: Prior diagnosis of heart failure (HF) is associated with increased length of hospital stay (LOS) and mortality from COVID-19. Associations between substance use, venous thromboembolism (VTE) or peripheral arterial disease (PAD) and its effects on LOS or mortality in patients with HF hospitalised with COVID-19 remain unknown. OBJECTIVE: This study identified risk

factors associated with poor in-hospital outcomes among patients with HF hospitalised with COVID-19. METHODS: Case-control study was conducted of patients with prior diagnosis of HF hospitalised with COVID-19 at an academic tertiary care centre from 1 January 2020 to 28 February 2021. Patients with HF hospitalised with COVID-19 with risk factors were compared with those without risk factors for clinical characteristics, LOS and mortality. Multivariate regression was conducted to identify multiple predictors of increased LOS and in-hospital mortality in patients with HF hospitalised with COVID-19. RESULTS: Total of 211 patients with HF were hospitalised with COVID-19. Women had longer LOS than men (9 days vs 7 days; p<0.001). Compared with patients without PAD or ischaemic stroke, patients with PAD or ischaemic stroke had longer LOS (7 days vs 9 days; p=0.012 and 7 days vs 11 days, p<0.001, respectively). Older patients (aged 65 and above) had increased in-hospital mortality compared with younger patients (adjusted OR: 1.04; 95% CI 1.00 to 1.07; p=0.036). Prior diagnosis of VTE increased mortality more than threefold in patients with HF hospitalised with COVID-19 (adjusted OR: 3.33; 95% CI 1.29 to 8.43; p=0.011). CONCLUSION: Vascular diseases increase LOS and mortality in patients with HF hospitalised with COVID-19.

[47] *Emrich IE, Heine GH, Schulze PC et al.* **Markers of cholesterol synthesis to cholesterol absorption across the spectrum of non-dialysis CKD: An observational study**. Pharmacol Res Perspect 2021; 9:e00801.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34128357

ABSTRACT

In dialysis patients, cholesterol-lowering therapy with statins is less effective than in other high-risk patients. This may be explained by a shift from cholesterol synthesis toward cholesterol absorption. In line, markers of cholesterol absorption-such as campesterol-better predict atherosclerotic cardiovascular events than markers of cholesterol synthesis-such as lathosterol-in dialysis patients. To test the association between markers of cholesterol absorption such as campesterol-and markers of cholesterol synthesis-such as lathosterol-against cardiovascular events in non-dialysis CKD patients. Altogether 251 patients those not on lipid-lowering agents were followed annually for the composite endpoint atherosclerotic cardiovascular disease (ASCVD) and all-cause death. During follow-up of 5.2 ± 2.1 years, 61 participants reached the primary endpoint atherosclerotic cardiovascular disease/all-cause death [ASCVD/D], 47 participants suffered from ASCVD, and 46 participants died. In univariate Cox regression analysis, campesterol/lathosterol ratio did not significantly predict ASCVD/D (HR 0.643; 0.358-1.155; 3rd vs. 1st tertile), all-cause death (HR 1.309; 0.604-2.838; 3rd vs. 1st tertile) nor ASCVD (HR 0.589; 0.311-1.118; 3rd vs. 1st tertile). We did not observe a shift from cholesterol synthesis to cholesterol absorption across the spectrum of non-dialysis CKD. Campesterol/lathosterol ratio did not predict future ASCVD or all-cause death in non-dialysis CKD.

[48] *McGraw-Senat CM, Dillard N, Guelda T et al.* **Bempedoic Acid: A First-in-Class Agent for Lowering Cholesterol Levels**. Sr Care Pharm 2021; 36:331-336.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34144722

ABSTRACT

Despite statin therapy being the cornerstone for the treatment of hypercholesterolemia, a significant number of patients do not tolerate statin therapy because of muscle-related adverse effects or cannot achieve their individual low-density lipoproteincholesterol (LDL-C) goals with statin therapy alone.

Several nonstatin agents have been evaluated for the management of LDL-C levels and reduction of cardiovascular (CV) risk in these patients, but there are some limitations with their use. Bempedoic acid is a novel nonstatin agent for the management of lipid disorders, via the inhibition of adenosine triphosphate citrate lyase (ACL). It was recently approved by the US Food and Drug Administration based on several phase III trials which showed promising results regarding safety and efficacy. Though CV outcome data are not available yet, bempedoic acid may be a useful adjunct therapy for select patients. The purpose of this review is to evaluate the major findings in these clinical trials and discuss the potential role of bempedoic acid in clinical practice and its use in older people.

[49] *de Macedo Ribeiro FRC, Ribeiro C, Tavoni TM et al.* **Disturbances of the transfer of cholesterol to high-density lipoprotein (HDL) in patients with peripheral artery disease with or without type 2 diabetes mellitus**. Vascular medicine (London, England) 2021:1358863x211021142.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34137646

ABSTRACT

INTRODUCTION: Low high-density lipoprotein (HDL)-cholesterol is frequent in patients with peripheral artery disease (PAD) and also in type 2 diabetes mellitus (T2DM), the major risk factor for PAD. The transfer of cholesterol from the other lipoproteins to HDL is an important aspect of HDL metabolism and function, and may contribute to atherogenic mechanisms that lead to PAD development. OBJECTIVE: The aim of this study was to investigate the status of cholesterol transfers in patients with PAD without or with T2DM. METHODS: Patients with PAD (n = 19), with PAD and T2DM (PAD + DM, n = 19), and healthy controls (n = 20), all paired for age, gender, and BMI were studied. Transfer of both forms of cholesterol, unesterified (UC) and esterified (EC), was performed by incubating plasma with a donor nanoemulsion containing radioactive UC and EC, followed by chemical precipitation and HDL radioactive counting. RESULTS: Low-density lipoprotein (LDL)-cholesterol and triglycerides were similar in the three groups. Compared to controls, HDL-C was lower in PAD + DM ($p < 0.05$), but not in PAD. Transfer of UC was lower in PAD + DM than in PAD and controls (4.18 ± 1.17%, 5.13 ± 1.44%, 6.59 ± 1.25%, respectively, $p < 0.001$). EC transfer tended to be lower in PAD + DM than in controls (2.96 ± 0.60 vs 4.12 ± 0.89%, $p = 0.05$). Concentrations of cholesteryl ester transfer protein (CETP) and lecithin-cholesterol acyltransferase (LCAT), both involved in HDL metabolism, were not different among the three groups. CONCLUSION: Deficient cholesterol transfer to HDL may play a role in PAD pathogenesis. Since UC transfer to HDL was lower in PAD + DM compared to PAD alone, it is possible that defective HDL metabolism may contribute to the higher PAD incidence in patients with T2DM.Keywords.

[50] *Yan K, Zhang T, Zha Y et al.* **Construction of point mutation rabbits using CRISPR/Cas9**. Zhejiang da xue xue bao. Yi xue ban = Journal of Zhejiang University. Medical sciences 2021; 50:229-238.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34137224

ABSTRACT

To establish a rabbit model of proprotein convertase subtilisin/kexin type9 () point mutation with CRISPR/Cas9 gene editing technique. According to the PubMed gene protein data, the PCSK9 protein functional regions of human and rabbit were analyzed by Blast. The 386S (Ser) amino acid functional region of human gene was homologous to the 485S of rabbit gene. Three small guide RNAs and one single-stranded donor oligonucleotide were designed according to the 485S base

substitution position and sequence analysis of rabbit gene. The synthetic small guide RNAs, Cas9 mRNA and single-stranded donor oligonucleotide were co-injected into the cytoplasm of rabbit fertilized eggs and the embryos were transferred into the pregnant rabbits. PCR, TA cloning and off-target analysis were performed on the F0 rabbits to identify whether the PCSK9 mutation was successful. Fifteen F0 rabbits were obtained. The sequencing results showed that one of them was PCSK9 point mutation homozygote and two of them were PCSK9 point mutation heterozygotes, and the mutation could be stably inherited. The rabbit model of PCSK9 point mutation was successfully constructed by CRISPR/Cas9 technique, which provides an animal model for exploring the molecular mechanism of impaired PCSK9 function and developing reliable and effective diagnosis and treatment measures.

[51] **[Expert consensus on the comprehensive management of blood pressure and dyslipidemia in Chinese hypertensive patients]**. Zhonghua xin xue guan bing za zhi 2021; 49:554-563.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34126722
ABSTRACT

[52] *Li YJ, Ma GS*. **[Clinical benefits and safety of low-level LDL-C in the new era of lipid-lowering]**. Zhonghua xin xue guan bing za zhi 2021; 49:548-553.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34126721
ABSTRACT

[53] *Wang XN, Wang F, Ye P et al.* **[Cross sectional study of familial hypercholesterolemia in dyslipidemia patients receiving lipid-lowering therapy: DYSIS-China subgroup analysis]**. Zhonghua xin xue guan bing za zhi 2021; 49:564-571.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34126723
ABSTRACT
Objectives: To analyze the incidence, blood lipid levels and cardiovascular disease of familial hypercholesterolemia (FH) in dyslipidemia patients receiving lipid-lowing therapy from the DYSIS-China. Methods: Dyslipidemia International Study-China (DYSIS-China) database was re-analyzed according to the criteria of "Chinese guidelines for prevention and treatment of dyslipidemia in adults-2016 version". DYSIS-China database included 25 317 dyslipidemia out-patients who received at least one lipid-lowering drug for at least three months. All the patients were divided into three groups: unlikely HF, possible FH and definite FH according to the Dutch Lipid Clinic Network diagnostic criteria. Age, gender, lipids levels, drug use and complications were compared among the three groups. Factors were compared between Possible FH group and definite FH group in terms of age stratification. Results: A total of 23 973 patients with dyslipidemia were included. The average age was (64.8±9.9) years, 11 757 patients were females (49.0%). The proportion of unlikely FH in the total population was 20 561 (85.7%), possible FH was 3294 (13.7%), and the definite FH was 118(0.5%). Patients in the definite FH group (58.3±8.5 years) was younger than in unlikely HF(65.3±9.8 years) and possible FH(61.8±9.9 years) group. LDL-C ((5.6±1.9) mmol/L) levels were significantly higher in definite FH group than in unlikely HF ((2.5±0.9) mmol/L) and possible FH ((4.3±1.0) mmol/L) group. TC ((7.4±1.8) mmol/L) levels were also significantly higher in definite FH group than in unlikely HF ((4.3±1.0) mmol/L) and possible FH ((6.0±1.0) mmol/L) group. Percent of

female sex, sedentary lifestyle and systolic blood pressure value were significantly higher in definite FH group than in other two groups (all P<0.05). Statin use was similar among the 3 groups. Prevalence of ischemic cardiomyopathy (70(59.3%)) was significantly higher in the definite FH group than in unlikely FH group7519 (36.6%) and possible FH group1149 (34.9%). The rate of hypertension (82 (69.5%)) was also significantly higher in the definite FH group than in unlikely FH group (2 063 (62.6%) and in possible FH group (13 928 (67.7%)). The possible FH group had the highest proportion of patients aged 55-64 years (1 146 (34.8%)), and the prevalence of hypertension 358 (76.8%), diabetes 189 (40.6%), ischemic heart disease 186 (39.9%), cerebrovascular disease 149 (32.0%) and heart failure 28 (6.0%) was the highest in patients over 75 years old. The definite FH group had the highest proportion of patients aged 55-64 years (49 (41.52%)), and the prevalence of ischemic heart disease (70 (59.3%)) was the highest in patients aged 45-54 years old group, there was no significant difference in the prevalence of diabetes,hypertension,heart failure,peripheral artery disease and cerebrovascular disease among different age groups. Conclusion: The detection rate of FH in Chinese patients with dyslipidemia is not low, the blood lipid level is poorly controlled, and the risk of cardiovascular disease is high in Chinses FH patients.

[54] *Yang F, Su GH, Cheng X*. **[Management of low-density lipoprotein cholesterol is fundamental for prevention and treatment of atherosclerotic cardiovascular disease]**. Zhonghua xin xue guan bing za zhi 2021; 49:638-642.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34126735
ABSTRACT

[55] *Zhang H, Ye PC, Wang XM et al.* **[The relationship between genotype of familial hypercholesterolemia and the efficacy of PCSK9 inhibitors]**. Zhonghua xin xue guan bing za zhi 2021; 49:572-579.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34126724
ABSTRACT
Objective: This study intends to explore the difference in the efficacy of PCSK9 inhibitors in patients with different FH phenotypes by analyzing the level of blood lipids before and after treatment with PCSK9 inhibitors in patients with familial hypercholesterolemia (FH) with different allele grades. Methods: Patients with FH phenotype, who admitted to Beijing Anzhen Hospital from January 2019 to October 2020, were enrolled. Age, sex and other clinical information were collected from enrolled, and the pathogenic genes were detected by the second generation sequencing technique. The patients were divided into five groups according to the number of alleles involved and the degree of gene damage: single allele-null mutation group, single allele-defect mutation group, multi-allele-null mutation group, multi-allele-defect mutation group and no major pathogenic gene mutation group. The results of blood lipids were collected before medication, 4-6 weeks of intensive statin treatment and one month after combined treatment with PCSK9 inhibitor (PCSK9i). The LDL-C level were compared among groups. ASCVD risk stratification was performed in all patients, and the proportion of LDL-C level reaching the corresponding risk stratification target value of each genotype group after treatment was analyzed. Results: A total of 66 patients with FH phenotype were included, including 47 males (71.2%) and 19 females (28.8%),the mean age was(43.1±13.4 years). There were 7 cases in single allele-null mutation group (10.6%), 25 cases in single allele-defect mutation group (37.9%), 8 cases in multi-allele-null mutation group (12.1%), 18 cases in multi-allele-defect mutation group

(27.3%) and 8 cases in no major pathogenic mutation group (12.1%). The degree of LDL-C reduction post combined PCSK9 inhibitor therapy was as follows: single allele mutation group>no major pathogenic mutation group>multi-allele mutation group, general distribution was in the range of 0-90.0%. Two groups of single allele mutation and no major pathogenic mutation group>50.0%>multi-allele mutation group. Under the combined treatment of PCSK9 inhibitors, the further decrease of LDL-C was in the order of single allele mutation group>non-major pathogenic mutant group>multi-allele mutation group. The efficacy of combined therapy on reducing LDL-C at 1 month after treatment decreased with the increase of baseline LDL-C level ($r = 0.46$, $P<0.001$) in patients with FH phenotype. In addition, the further decrease of LDL-C level post high-intensity statin therapy combined with PCSK9 inhibitors decreased with the increase of baseline LDL-C levels ($r = 0.40$, $P<0.001$). The degree of LDL-C decrease was high and stable by statin combined with PCSK9 inhibitor therapy in single allele mutation group. In the single allele-defect mutant group, the decrease of LDL-C increased with the increase of baseline LDL-C level post intensive statin treatment and combined PCSK9 inhibitor treatment (($r=0.54$, $P=0.009$); $r=0.45$,$P=0.030$), and the further decrease of LDL-C level decreased with the increase of baseline LDL-C level in single allele-defect mutant group post combined therapy with PCSK9 inhibitor ($r=0.43$, $P=0.040$). The decrease of LDL-C in patients with the multi-allele mutation group varied with different pathogenic gene loci and combinations post combined therapy with PCSK9 inhibitor. There was no significant difference in the level of blood lipids between the group without major pathogenic gene mutation and the group with single allele mutation before and after treatment. The percentage of patients achieving LDL-C goals with different genotypes of phenotypic FH were as follows: single allele mutation group (86.7%), non-major pathogenic mutant group (75.0%) and multi-allele mutation grou (<5.0%). Conclusions: All patients with different FH phenotypes could benefit from the intensive lipid-lowering therapy with statins and PCSK9 inhibitors, however, there are significant differences in the efficacy of lowering LDL-C in Chinese patients with FH phenotype with different molecular etiologies. Therefore, the pathogenic gene analysis may suggest the lipid-lowering effect of PCSK9 inhibitors in patients with FH.

[56] *Zhang Y, Pan YJ, Yan JC*. **[Update on the association between endothelial-mesenchymal transition and vulnerable plaque]**. Zhonghua xin xue guan bing za zhi 2021; 49:632-637.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34126734
ABSTRACT

[57] *Zhao SP*. **[Strictly management of blood lipids as the source control of atherosclerotic cardiovascular disease in terms of prevention and treatment]**. Zhonghua xin xue guan bing za zhi 2021; 49:545-547.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34126720
ABSTRACT