[1] *Aschenbrenner DS*. **Statins No Longer Contraindicated in Pregnancy**. The American journal of nursing 2021; 121:22.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34673690
ABSTRACT
The labeling of statins has been revised to remove the contraindication for use during pregnancy.For a select few women at high risk for cardiovascular events, statins may provide more benefit than risk, even during pregnancy. Most women do not have this high risk, however, and should still avoid statins during pregnancy.

[2] *Smith DD, Costantine MM*. **Reply: Timing of pravastatin initiation for preeclampsia prevention**. American journal of obstetrics and gynecology 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34666054
ABSTRACT

[3] *Aldika Akbar MI, Yosediputra A, Eri Pratama R et al.* **INOVASIA Study: A Randomized Open Controlled Trial to Evaluate Pravastatin to Prevent Preeclampsia and its Effects on sFlt1/PLGF Levels**. Am J Perinatol 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34666379
ABSTRACT
Objectives To evaluate the effect of pravastatin to prevent preeclampsia (PE) in pregnant women at a high risk of developing preeclampsia and the maternal and perinatal outcomes and the sFlt1/PLGF ratio. Study Design This is an open labelled RCT part of INOVASIA trial. Pregnant women at a high risk of developing PE were recruited and randomized into an intervention group (40) and a control group (40). The inclusion criteria consisted of pregnant women with positive clinical risk factor and abnormal uterine artery doppler examination at 10-20 weeks gestational age. The control group received low dose aspirin (80 mg/day) and calcium (1 g/day), while the intervention group received additional pravastatin (20 mg twice daily) starting from 14-20 weeks gestation until delivery. Research blood samples were collected before the first dose of pravastatin and before delivery. The main outcome was the rate of maternal preeclampsia, maternal-perinatal outcomes, and sFlt-1, PLGF, sFlt-1/PlGF ratio and sEng levels. Results The rate of preeclampsia was (non-significantly) lower in the pravastatin group compared with the control group (17.5% vs 35%). The pravastatin group also had a (non-significant) lower rate of severe preeclampsia, HELLP syndrome, acute kidney injury and severe hypertension. The rate of (iatrogenic) preterm delivery was significantly (p=0.048) lower in the pravastatin group (n=4) compared with the controls (n=12). Neonates in the pravastatin group had significantly higher birthweights (2931 + 537 vs 2625 + 872 g; p=0.006), lower Apgar scores < 7 (2.5 vs 27.5%, p=0.002), composite neonatal morbidity (0 vs 20%, p=0.005) and NICU admission rates (0 vs 15%, p=0.026). All biomarkers show a significant deterioration in the control group compared with non significant changes in the pravastatin group. Conclusions Pravastatin holds promise in the secondary prevention of preeclampsia and placenta-mediated adverse perinatal outcomes by improving the angiogenic imbalance.

[4] *Stock JK*. **Global Familial Hypercholesterolaemia Studies Collaboration (FHSC)**. Atherosclerosis 2021; 337:57-58.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34686380

ABSTRACT

[5] *Yang M, Geng CA, Liu X, Guan M*. **Lipid Disorders in NAFLD and Chronic Kidney Disease**. Biomedicines 2021; 9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34680522

ABSTRACT

Nonalcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver dysfunction and is characterized by exaggerated lipid accumulation, inflammation and even fibrosis. It has been shown that NAFLD increases the risk of other chronic diseases, particularly chronic kidney disease (CKD). Lipid in excess could lead to liver and kidney lesions and even end-stage disease through diverse pathways. Dysregulation of lipid uptake, oxidation or de novo lipogenesis contributes to the toxic effects of ectopic lipids which promotes the development and progression of NAFLD and CKD via triggering oxidative stress, apoptosis, pro-inflammatory and profibrotic responses. Importantly, dyslipidemia and release of pro-inflammatory cytokines caused by NAFLD (specifically, nonalcoholic steatohepatitis) are considered to play important roles in the pathological progression of CKD. Growing evidence of similarities between the pathogenic mechanisms of NAFLD and those of CKD has attracted attention and urged researchers to discover their common therapeutic targets. Here, we summarize the current understanding of molecular aberrations underlying the lipid metabolism of NAFLD and CKD and clinical evidence that suggests the relevance of these pathways in humans. This review also highlights the orchestrated inter-organ cross-talk in lipid disorders, as well as therapeutic options and opportunities to counteract NAFLD and CKD.

[6] *Skrzypiec-Spring M, Sapa-Wojciechowska A, Haczkiewicz-Leśniak K et al.* **HMG-CoA Reductase Inhibitor, Simvastatin Is Effective in Decreasing Degree of Myocarditis by Inhibiting Metalloproteinases Activation**. Biomolecules 2021; 11.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34680049

ABSTRACT

BACKGROUND: Acute myocarditis often progresses to heart failure because there is no effective, etiology-targeted therapy of this disease. Simvastatin has been shown to be cardioprotective by decreasing matrix metalloproteinases' (MMPs) activity. The study was designed to determine whether simvastatin inhibits MMPs activity, decreases the severity of inflammation and contractile dysfunction of the heart in experimental autoimmune myocarditis (EAM). METHODS: Simvastatin (3 or 30 mg/kg/day) was given to experimental rats with EAM by gastric gavage for 21 days. Then transthoracic echocardiography was performed, MMPs activity and troponin I level were determined and tissue samples were assessed under a light and transmission electron microscope. RESULTS: Hearts treated with simvastatin did not show left ventricular enlargement. As a result of EAM, there was an enhanced activation of MMP-9, which was significantly reduced in the high-dose simvastatin group compared to the low-dose group. It was accompanied by prevention of myofilaments degradation and reduction of severity of inflammation. CONCLUSIONS: The cardioprotective effects of simvastatin in the acute phase of EAM are, at least in part, due to its ability to decrease MMP-9 activity and subsequent decline in myofilaments degradation and suppression of inflammation. These effects were achieved in doses equivalent to therapeutic doses in humans.

[7] *Han KT, Choi DW, Kim S*. **Regional and income disparities in treatment and drug adherence of patients with dyslipidemia: a retrospective cohort study in South Korea, 2003-2015**. BMC geriatrics 2021; 21:585.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34674649
ABSTRACT
BACKGROUNDS: Health disparities represent a major public health problem that needs to be addressed, and a variety of factors, including geographical location and income, can contribute to these disparities. Although previous studies have suggested that health differs by region and income, evidence on the difference in treatment rate is relatively insufficient. To identify differences in prescription rates by region and income in patients with dyslipidemia. METHODS: Using data from the National Health Insurance Service senior cohort, we included older adults who were diagnosed with dyslipidemia in Korea from 2003 to 2015. Overall prescription rate was determined for patients with dyslipidemia. In addition, medication possession ratio and a defined daily dose were analyzed in patients who were prescribed statins. A generalized estimating equation Poisson model was used to assess differences in prescription rates. RESULTS: Patients living in rural areas (Chungcheong-do, Jeolla-do, and Gyeongsang-do) had a significantly higher prescription rate than those in metropolitan cities. Unlike the prescription rate, the drug adherence was significantly higher in Seoul, Gyeonggi-do, and Gangwon-do but lower in Jeolla-do and Gyeongsang-do than in metropolitan cities. Patients with low income had lower prescription rates than those with high income, but this difference was not statistically significant. CONCLUSION: Our findings demonstrate differences in the treatment rates of patients with dyslipidemia by region and income. Appropriate interventions are needed in vulnerable regions and groups to increase the treatment rate for patients with dyslipidemia.

[8] *Holder TA, Gutierrez JA, Aday AW*. **Medical Management of Peripheral Artery Disease**. Cardiol Clin 2021; 39:471-482.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34686260
ABSTRACT
Peripheral artery disease is a highly morbid yet undertreated atherosclerotic disease. The cornerstones of peripheral artery disease therapy consist of smoking cessation, lipid-lowering therapy, and hypertension treatment. More recently, clinical trials have demonstrated that novel antiplatelet and antithrombotic therapies reduce the risk of both cardiovascular and limb events in this patient population. In this review, we highlight the components of optimal medical therapy of peripheral artery disease and the evidence base for these therapies.

[9] *Peterson KA, Kaur G, Gianos E et al.* **Challenges in Optimizing Lipid Management in Women**. Cardiovascular drugs and therapy / sponsored by the International Society of Cardiovascular Pharmacotherapy 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34661802
ABSTRACT
While there are physiologic differences in lipid metabolism in men and women, pharmacologic therapy is very effective in both with similar management strategies recommended in the current guidelines for the management of dyslipidemia. Despite similar guidelines for treatment, studies have shown that women have worse control of dyslipidemia than their male counterparts. This may stem from multiple contributing factors including underestimation of cardiovascular disease risk in women,

decreased prescription and utilization of lipid-lowering therapies, decreased medication adherence, and higher risk of statin intolerance, all of which may contribute to lower attainment of lipid targets. Furthermore, heart disease is the leading cause of mortality in women, with heart disease noted an average of 7-10 years later than in men. This has historically led to the misperception that women are protected from heart disease and can be treated less aggressively. In fact, traditional risk factors for atherosclerotic cardiovascular disease often impact risk in women to a greater extent than they do in men. Unique risk factors such as pregnancy-related disorders also contribute to the level of risk and therefore warrant consideration in risk stratification. This review summarizes the efficacy of contemporary lipid-lowering therapies in women versus men and discusses the challenges that arise with lipid management in women along with potential ways to tackle these obstacles.

[10] *Barraclough JY, Patel S, Yu J et al.* **The Role of Sodium Glucose Cotransporter-2 Inhibitors in Atherosclerotic Cardiovascular Disease: A Narrative Review of Potential Mechanisms**. Cells 2021; 10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34685677
ABSTRACT
Sodium glucose cotransporter 2 (SGLT2) inhibitors are a class of medication with broad cardiovascular benefits in those with type 2 diabetes, chronic kidney disease, and heart failure. These include reductions in major adverse cardiac events and cardiovascular death. The mechanisms that underlie their benefits in atherosclerotic cardiovascular disease (ASCVD) are not well understood, but they extend beyond glucose lowering. This narrative review summarises the ASCVD benefits of SGLT2 inhibitors seen in large human outcome trials, as well as the mechanisms of action explored in rodent and small human studies. Potential pathways include favourable alterations in lipid metabolism, inflammation, and endothelial function. These all require further investigation in large human clinical trials with mechanistic endpoints, to further elucidate the disease modifying benefits of this drug class and those who will benefit most from it.

[11] *Mihalj M, Heinisch PP, Huber M et al.* **Effect of Perioperative Lipid Status on Clinical Outcomes after Cardiac Surgery**. Cells 2021; 10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34685697
ABSTRACT
Patients undergoing cardiac surgery are at increased cardiovascular risk, which includes altered lipid status. However, data on the effect of cardiac surgery and cardiopulmonary bypass (CPB) on plasma levels of key lipids are scarce. We investigated potential effects of CPB on plasma lipid levels and associations with early postoperative clinical outcomes. This is a prospective bio-bank study of patients undergoing elective cardiac surgery at our center January to December 2019. The follow-up period was 1 year after surgery. Blood sampling was performed before induction of general anesthesia, upon weaning from cardiopulmonary bypass (CPB), and on the first day after surgery. Clinical end points included the incidence of postoperative stroke, myocardial infarction, and death of any cause at 30 days after surgery as well as 1-year all-cause mortality. A total of 192 cardiac surgery patients (75% male, median age 67.0 years (interquartile range 60.0-73.0), median BMI 26.1 kg/m(2) (23.7-30.4)) were included. A significant intraoperative decrease in plasma levels compared with preoperative levels (all $p < 0.0001$) was observed for total cholesterol (TC) (Cliff's delta d: 0.75 (0.68-0.82; 95% CI)), LDL-Cholesterol (LDL-C) (d: 0.66 (0.57-0.73)) and HDL-Cholesterol (HDL-C) (d:

0.72 (0.64-0.79)). At 24h after surgery, the plasma levels of LDL-C (d: 0.73 (0.650.79)) and TC (d: 0.77 (0.69-0.82)) continued to decrease compared to preoperative levels, while the plasma levels of HDL-C (d: 0.46 (0.36-0.55)) and TG (d: 0.40 (0.29-0.50)) rebounded, but all remained below the preoperative levels ($p < 0.001$). Mortality at 30 days was 1.0% (N = 2/192), and 1-year mortality was 3.8% (N = 7/186). Postoperative myocardial infarction occurred in 3.1% of patients (N = 6/192) and postoperative stroke in 5.8% (N = 11/190). Adjusting for age, sex, BMI, and statin therapy, we noted a protective effect of postoperative occurrence of stroke for pre-to-post-operative changes in TC (adjusted odds ratio (OR) 0.29 (0.07-0.90), p = 0.047), in LDL-C (aOR 0.19 (0.03-0.88), p = 0.045), and in HDL-C (aOR 0.01 (0.00-0.78), p = 0.039). No associations were observed between lipid levels and 1-year mortality. In conclusion, cardiac surgery induces a significant sudden drop in levels of key plasma lipids. This effect was pronounced during the operation, and levels remained significantly lowered at 24 h after surgery. The intraoperative drops in LDL-C, TC, and HDL-C were associated with a protective effect against occurrence of postoperative stroke in adjusted models. We demonstrate that the changes in key plasma lipid levels during surgery are strongly correlated, which makes attributing the impact of each lipid to the clinical end points, such as postoperative stroke, a challenging task. Large-scale analyses should investigate additional clinical outcome measures.

[12] *Sampedro-Nuñez M, Aguirre-Moreno N, García-Fraile Fraile L et al.* **Finding answers in lipid profile in COVID-19 patients**. Endocrine 2021; 74:443-454.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34668172

ABSTRACT

INTRODUCTION: A small percentage of patients will develop a severe form of COVID-19 caused by SARS-CoV-2 infection. Thus, it is important to predict the potential outcomes identifying early markers of poor prognosis. In this context, we evaluated the association of SARS-CoV-2 infection with lipid abnormalities and their role in prognosis. METHODS: Single-center, retrospective, observational study of COVID-19 patients admitted from March to October 2020. Clinical and laboratory data, comorbidities, and treatments for COVID-19 were evaluated. Main outcomes including intensive care unit (ICU) admission and mortality were analyzed with a multivariable Cox proportional hazards regression model. RESULTS: We selected 1489 from a total of 2038 consecutive patients with confirmed COVID-19, who had a complete lipid profile before ICU admission. During the follow-up performed in 1109 patients, we observed a decrease in T-c, HDL-c, and LDL-c in 28.6%, 42.9%, and 30.4% of patients, respectively, and an increase in TG in 76.8%. The decrease of both T-c and HDL- c was correlated with a decrease in albumin levels ($r = 0.39$ and $r = 0.37$, respectively). Kaplan-Meier survival curves found an increased ICU admission in patients with lower T-c (HR 0.55, CI 0.36-0.86), HDL-c (HR 0.61, CI 0.45-0.84), and LDL-c (HR 0.85, CI 0.74-0.97). Higher values of T-c (HR 0.45, CI 0.36-0.57), HDL-c (HR 0.66, CI 0.54-0.81), and LDL-c (HR 0.86, CI 0.78-0.94) showed a protective effect on mortality. CONCLUSIONS: Abnormalities in lipid profile are a frequent complication of SARS-CoV-2 infection and might be related to morbidity and mortality. FUNDING: Proyectos de Investigación en Salud (FIS) and cofinanced by FEDER.

[13] Warden BA, Fazio S, Shapiro MD. Familial Hypercholesterolemia: Genes and Beyond. In: Endotext. Edited by: Feingold KR, Anawalt B, Boyce A *et al.* South Dartmouth (MA): MDText.com, Inc.

[14] *Wadström BN, Wulff AB, Pedersen KM et al.* **Elevated remnant cholesterol increases the risk of peripheral artery disease, myocardial infarction, and ischaemic stroke: a cohort-based study**. European heart journal 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34661640

ABSTRACT

AIMS : The atherogenic potential of cholesterol in triglyceride-rich lipoproteins, also called remnant cholesterol, is being increasingly acknowledged. Elevated remnant cholesterol is associated with increased risk of myocardial infarction and ischaemic stroke. We tested the hypothesis that elevated remnant cholesterol is also associated with increased risk of peripheral artery disease (PAD). METHODS AND RESULTS : We studied 106 937 individuals from the Copenhagen General Population Study recruited in 2003-15. During up to 15 years of follow-up, 1586 were diagnosed with PAD, 2570 with myocardial infarction, and 2762 with ischaemic stroke. We also studied 13 974 individuals from the Copenhagen City Heart Study recruited in 1976-78. During up to 43 years of follow-up, 1033 were diagnosed with PAD, 2236 with myocardial infarction, and 1976 with ischaemic stroke. Remnant cholesterol was calculated from a standard lipid profile. Diagnoses were from Danish nationwide health registries. In the Copenhagen General Population Study, elevated remnant cholesterol levels were associated with higher risk of PAD, up to a multivariable adjusted hazard ratio (HR) of 4.8 (95% confidence interval 3.1-7.5) for individuals with levels ≥1.5 mmol/L (58 mg/dL) vs. <0.5 mmol/L (19 mg/dL). Corresponding results were 4.2 (2.9-6.1) for myocardial infarction and 1.8 (1.4-2.5) for ischaemic stroke. In the Copenhagen City Heart Study, corresponding HRs were 4.9 (2.9-8.5) for PAD, 2.6 (1.8-3.8) for myocardial infarction, and 2.1 (1.5-3.1) for ischaemic stroke. CONCLUSION : Elevated remnant cholesterol is associated with a five-fold increased risk of PAD in the general population, higher than for myocardial infarction and ischaemic stroke.

[15] *Jin H, He J, Dong C et al.* **Altered Lipid Profile Is a Risk Factor for the Poor Progression of COVID-19: From Two Retrospective Cohorts**. Frontiers in cellular and infection microbiology 2021; 11:712530.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34660338

ABSTRACT

BACKGROUND: The coronavirus disease 2019 (COVID-19) pandemic has spread worldwide. However, the impact of baseline lipid profile on clinical endpoints in COVID-19 and the potential effect of COVID-19 on lipid profile remain unclear. METHODS: In this retrospective cohort study, we consecutively enrolled 430 adult COVID-19 patients from two Chinese hospitals (one each in Chengdu and Wuhan). The lipid profile before admission and during the disease course and the clinical endpoint including in-hospital death or oropharyngeal swab test positive again (OSTPA) after discharge were collected. We used Kaplan-Meier and Cox regression to explore the lipid risk factors before admission associated with endpoints. Then, we assessed the lipid level change along with the disease course to determine the relationship between pathology alteration and the lipid change. RESULTS: In the Chengdu cohort, multivariable Cox regression showed that low-density lipoprotein cholesterol (LDL-C) dyslipidemia before admission was associated with OSTPA after discharge for COVID-19 patients (RR: 2.51, 95% CI: 1.19, 5.29, p = 0.006). In the Wuhan cohort, the patients with triglyceride (TG) dyslipidemia had an increased risk of in-hospital death (RR: 1.92, 95% CI: 1.08, 3.60, p = 0.016). In addition, in both cohorts, the lipid levels gradually decreased in the in-hospital death or OSTPA subgroups since admission. On admission, we also noticed the relationship between

the biomarkers of inflammation and the organ function measures and this lipid level in both cohorts. For example, after adjusting for age, sex, comorbidities, smoking, and drinking status, the C-reactive protein level was negatively associated with the TC lipid level [β (SE) = -0.646 (0.219), p = 0.005]. However, an increased level of alanine aminotransferase, which indicates impaired hepatic function, was positively associated with total cholesterol (TC) lipid levels in the Chengdu cohort [β (SE) = 0.633 (0.229), p = 0.007]. CONCLUSIONS: The baseline dyslipidemia should be considered as a risk factor for poor prognosis of COVID-19. However, lipid levels may be altered during the COVID-19 course, since lipidology may be distinctly affected by both inflammation and organic damage for SARS-CoV-2.

[16] *Melhem AL, Chourasia MK, Bigossi M et al.* **Common Statin Intolerance Variants in ABCB1 and LILRB5 Show Synergistic Effects on Statin Response: An Observational Study Using Electronic Health Records**. Frontiers in genetics 2021; 12:713181.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34659336

ABSTRACT

Background: Statin intolerance impacts approximately 10% of statin users, with side effects ranging from mild myalgia to extreme intolerance resulting in myopathy and rhabdomyolysis. Statin intolerance results in poor adherence to therapy and can impact statin efficacy. Many genetic variants are associated with statin intolerance. The effect of these variants on statin efficacy has not been systematically explored. Methods: Using longitudinal electronic health records and genetic biobank data from Tayside, Scotland, we examined the effect of seven genetic variants with previously reported associations with simvastatin or atorvastatin intolerance on the outcome of statin response. Statin response was measured by the reduction achieved when comparing pre- and post-statin non-high-density lipoprotein-cholesterol (non-HDL-C). Post-treatment statin response was limited to non-HDL-C measured within 6months of therapy initiation. Univariate and multivariable linear regression models were used to assess the main and adjusted effect of the variants on statin efficacy. Results: Around 9,401 statin users met study inclusion criteria, of whom 8,843 were first prescribed simvastatin or atorvastatin. The average difference in post-treatment compared to pre-treatment non-HDL-cholesterol was 1.45 (±1.04) mmol/L. In adjusted analyses, only two variants, one in the gene ATP-binding cassette transporter B1 (ABCB1; rs1045642), and one in leukocyte immunoglobulin like receptor B5 (LILRB5; rs12975366), were associated with statin efficacy. In ABCB1, homozygous carriers of the C allele at rs1045642 had 0.06mmol/L better absolute reduction in non-HDL-cholesterol than carriers of the T allele (95% CI: 0.01, 0.1). In LILRB5 (rs12975366), carriers of the C allele had 0.04mmol/L better absolute reduction compared to those homozygous for the T allele (95% CI: 0.004, 0.08). When combined into a two-variant risk score, individuals with both the rs1045642-CC genotype and the rs12975366-TC or CC genotype had a 0.11mmol/L greater absolute reduction in non-HDL-cholesterol compared to those with rs1045642-TC or TT genotype and the rs12975366-TT genotype (95% CI: 0.05, 0.16; p<0.001). Conclusion: We report two genetic variants for statin adverse drug reactions (ADRs) that are associated with statin efficacy. While the ABCB1 variant has been shown to have an association with statin pharmacokinetics, no similar evidence for LILRB5 has been reported. These findings highlight the value of genetic testing to deliver precision therapeutics to statin users.

[17] *Argnani L, Zanetti A, Carrara G et al.* **Rheumatoid Arthritis and Cardiovascular Risk: Retrospective Matched-Cohort Analysis Based on the RECORD Study of the Italian Society for Rheumatology**. Frontiers in medicine 2021; 8:745601.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34676228
ABSTRACT
Background: Rheumatoid arthritis (RA) is associated with an increase in cardiovascular (CV) risk. This issue maybe not only explained by a genetic component, as well as by the traditional CV risk factors, but also by an underestimation and undertreatment of concomitant CV comorbidities. Method: This was a retrospective matched-cohort analysis in the Italian RA real-world population based on the healthcare-administrative databases to assess the CV risk factors and incidence of CV events in comparison with the general population. Persistence and adherence to the CV therapy were also evaluated in both groups. Results: In a RA cohort (N = 21,201), there was a greater prevalence of hypertension and diabetes with respect to the non-RA subjects (N = 249,156) (36.9 vs. 33.4% and 10.2 vs. 9.6%, respectively), while dyslipidemia was more frequent in the non-RA group (15.4 vs. 16.5%). Compared with a non-RA cohort, the patients with RA had a higher incidence of atrial fibrillation (incidence rate ratio, IRR 1.28), heart failure (IRR 1.53), stroke (IRR 1.19), and myocardial infarction (IRR 1.48). The patients with RA presented a significantly lower persistence rate to glucose-lowering and lipid-lowering therapies than the controls (odds ratio, OR 0.73 [95% CI 0.6-0.8] and OR 0.82 [0.8-0.9], respectively). The difference in the adherence to glucose-lowering therapy was significant (OR 0.7 [0.6-0.8]), conversely no statistically significant differences emerged regarding the adherence to lipid-lowering therapy (OR 0.89 [95% CI 0.8-1.0]) and anti-hypertensive therapy (OR 0.96 [95% CI 0.9-1.0]). Conclusion: The patients with RA have a higher risk of developing CV events compared with the general population, partially explained by the excess and undertreatment of CV risk factors.

[18] *Leong XF*. **Lipid Oxidation Products on Inflammation-Mediated Hypertension and Atherosclerosis: A Mini Review**. Front Nutr 2021; 8:717740.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34660660
ABSTRACT
Cardiovascular diseases such as hypertension and atherosclerosis are the common causes of mortality in developed and developing countries. Repeated heating of the dietary oil is a common practice to reduce cost during food preparation. When the cooking oil is heated at high temperatures, production of free radicals augments the oxidative degradation of lipids and depletes the natural antioxidant contents of the cooking oil. Chronic intake of foods prepared using reheated oil could impair antioxidant capacity, leading to oxidative stress and inflammation. This review aims to summarize the current evidence of lipid oxidation products on hypertension and atherosclerosis via inflammatory pathway. In particular, toxic lipid oxidation products such as malondialdehyde and 4-hydroxy-2-nonenal are taken into account. Understanding the signaling pathways underlying the pathology associated with the lipid oxidation-derived aldehydes may be useful to develop therapeutic strategies for the prevention of inflammatory-related cardiovascular complications.

[19] *Dlouha D, Blaha M, Rohlova E et al.* **Multiplex Protein Biomarker Profiling in Patients with Familial Hypercholesterolemia**. Genes 2021; 12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34680994

ABSTRACT
Familial hypercholesterolemia (FH), is an autosomal dominant disorder caused by mutations in the LDLR, APOB, PCSK9, and APOE genes and is characterized by high plasma levels of total and low-density lipoprotein (LDL) cholesterol. Our study aimed to analyze the influences of two different therapies on a wide spectrum of plasma protein biomarkers of cardiovascular diseases. Plasma from FH patients under hypolipidemic therapy (N = 18; men = 8, age 55.4 ± 13.1 years) and patients under combined long-term LDL apheresis/hypolipidemic therapy (N = 14; men = 7; age 58.0 ± 13.6 years) were analyzed in our study. We measured a profile of 184 cardiovascular disease (CVD) associated proteins using a proximity extension assay (PEA). Hypolipidemic therapy significantly (all $p < 0.01$) influenced 10 plasma proteins (TM, DKK1, CCL3, CD4, PDGF subunit B, AGRP, IL18, THPO, and LOX1 decreased; ST2 increased). Under combined apheresis/hypolipidemic treatment, 18 plasma proteins (LDLR, PCSK9, MMP-3, GDF2, CTRC, SORT1, VEGFD, IL27, CCL24, and KIM1 decreased; OPN, COL1A1, KLK6, IL4RA, PLC, TNFR1, GLO1, and PTX3 increased) were significantly affected (all $p < 0.006$). Hypolipidemic treatment mainly affected biomarkers involved in vascular endothelial maintenance. Combined therapy influenced proteins that participate in cholesterol metabolism and inflammation.

[20] *Meroni M, Longo M, Lombardi R et al.* **Low Lipoprotein(a) Levels Predict Hepatic Fibrosis in Patients With Nonalcoholic Fatty Liver Disease**. Hepatology communications 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34677008

ABSTRACT
Dyslipidemia and cardiovascular complications are comorbidities of nonalcoholic fatty liver disease (NAFLD), which ranges from simple steatosis to nonalcoholic steatohepatitis, fibrosis, and cirrhosis up to hepatocellular carcinoma. Lipoprotein(a) (Lp(a)) has been associated with cardiovascular risk and metabolic abnormalities, but its impact on the severity of liver damage in patients with NAFLD remains to be clarified. Circulating Lp(a) levels were assessed in 600 patients with biopsy-proven NAFLD. The association of Lp(a) with liver damage was explored by categorizing serum Lp(a) into quartiles. The receiver operating characteristic curve was used to analyze the accuracy of serum Lp(a) in hepatic fibrosis prediction. Hepatic expression of lipoprotein A (LPA) and of genes involved in lipid metabolism and fibrogenic processes were evaluated by RNA sequencing in a subset of patients with NAFLD for whom Lp(a) dosage was available (n = 183). In patients with NAFLD, elevated Lp(a) levels were modestly associated with circulating lipids, carotid plaques, and hypertension ($P < 0.05$). Conversely, patients with low serum Lp(a) displayed insulin resistance ($P < 0.05$), transaminase elevation ($P < 0.05$), and increased risk of developing severe fibrosis ($P = 0.007$) and cirrhosis ($P = 0.002$). In addition, the diagnostic accuracy of Lp(a) in predicting fibrosis increased by combining it with transaminases (area under the curve fibrosis stage 4, 0.87; $P < 0.0001$). Hepatic LPA expression reflected serum Lp(a) levels ($P = 0.018$), and both were reduced with the progression of NAFLD ($P < 0.05$). Hepatic LPA messenger RNA levels correlated with those of genes involved in lipoprotein release, lipid synthesis, and fibrogenesis ($P < 0.05$). Finally, transmembrane 6 superfamily member 2 (TM6SF2) rs58542926, apolipoprotein E (ApoE) rs445925, and proprotein convertase subtilisin/kexin type 9 (PCSK9) rs7552841, known variants that modulate circulating lipids, may influence serum Lp(a) levels ($P < 0.05$). Conclusion: Circulating Lp(a) combined with transaminases may represent a novel noninvasive biomarker to predict advanced fibrosis in patients with NAFLD.

[21] *Rizos CV, Skoumas I, Rallidis L et al.* **LDL cholesterol target achievement in heterozygous familial hypercholesterolemia patients according to 2019 ESC/EAS lipid guidelines: Implications for newer lipid-lowering treatments**. International journal of cardiology 2021; 345:119-124.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34687802

ABSTRACT

BACKGROUND: The 2019 European guidelines (ESC/EAS) for the treatment of dyslipidaemias recommend more aggressive targets for low-density lipoprotein cholesterol (LDL-C) in patients with familial hypercholesterolemia (FH). Current lipid-lowering treatment is often inadequate to achieve these targets. METHODS: Data from the HELLAS-FH registry were analysed to assess achievement of LDL-C targets in adults with FH based on the 2019 ESC/EAS guidelines. In patients who had not achieved LDL-C target, the maximally reduced LDL-C value was calculated after theoretical switch to rosuvastatin/ezetimibe 40/10 mg/day. The percentage of patients who remained candidates for proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9i) was then calculated. RESULTS: Patients (n = 1694, mean age 50.8 ± 14.7 years) had LDL-C levels 242 ± 71 mg/dL (6.3 ± 1.8 mmol/L) at diagnosis. Most treated patients were receiving statins (97.5%) and about half were on additional ezetimibe (47.5%). Based on the 2019 ESC/EAS guidelines the percentage of patients achieving LDL-C goals was only 2.7%. Following theoretical up titration to rosuvastatin/ezetimibe 40/10 mg, LDL-C target achievement rate would increase to 5.9%. In this scenario, most patients (55.9%) would be eligible for PCSK9i treatment. Following theoretical administration of a PCSK9i, LDL-C target achievement rate would rise to 57.6%. However, 42.4% of patients would still be eligible for further LDL-C lowering treatment. CONCLUSIONS: Most FH patients do not reach new LDL-C targets even if on maximum intensity statin/ezetimibe treatment. In this case, more than half of FH patients are candidates for PCSK9i therapy and a considerable proportion may still require additional LDL-C lowering.

[22] *Petersen-Uribe Á, Kremser M, Rohlfing AK et al.* **Platelet-Derived PCSK9 Is Associated with LDL Metabolism and Modulates Atherothrombotic Mechanisms in Coronary Artery Disease**. International journal of molecular sciences 2021; 22.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34681838

ABSTRACT

Platelets play a significant role in atherothrombosis. Proprotein convertase subtilisin/kexin type 9 (PCSK9) is critically involved in the regulation of LDL metabolism and interacts with platelet function. The effect of PCSK9 in platelet function is poorly understood. The authors of this article sought to characterize platelets as a major source of PCSK9 and PCSK9's role in atherothrombosis. In a large cohort of patients with coronary artery disease (CAD), platelet count, platelet reactivity, and platelet-derived PCSK9 release were analyzed. The role of platelet PCSK9 on platelet and monocyte function was investigated in vitro. Platelet count and hyper-reactivity correlated with plasma LDL in CAD. The circulating platelets express on their surface and release substantial amounts of PCSK9. Release of PCSK9 augmented platelet-dependent thrombosis, monocyte migration, and differentiation into macrophages/foam cells. Platelets and PCSK9 accumulated in tissue derived from atherosclerotic carotid arteries in areas of macrophages. PCSK9 inhibition reduced platelet activation and platelet-dependent thrombo-inflammation. The authors identified platelets as a source of PCSK9 in CAD, which may have an impact on LDL metabolism. Furthermore, platelet-derived PCSK9 contributes to

atherothrombosis, and inhibition of PCSK9 attenuates thrombo-inflammation, which may contribute to the reported beneficial clinical effects.

[23] *Theofilis P, Sagris M, Antonopoulos AS et al.* **Inflammatory Mediators of Platelet Activation: Focus on Atherosclerosis and COVID-19**. International journal of molecular sciences 2021; 22.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34681830
ABSTRACT
BACKGROUND: Atherosclerotic cardiovascular diseases are characterized by a dysregulated inflammatory and thrombotic state, leading to devastating complications with increased morbidity and mortality rates. SUMMARY: In this review article, we present the available evidence regarding the impact of inflammation on platelet activation in atherosclerosis. Key messages: In the context of a dysfunctional vascular endothelium, structural alterations by means of endothelial glycocalyx thinning or functional modifications through impaired NO bioavailability and increased levels of von Willebrand factor result in platelet activation. Moreover, neutrophil-derived mediators, as well as neutrophil extracellular traps formation, have been implicated in the process of platelet activation and platelet-leukocyte aggregation. The role of pro-inflammatory cytokines is also critical since their receptors are also situated in platelets while TNF-α has also been found to induce inflammatory, metabolic, and bone marrow changes. Additionally, important progress has been made towards novel concepts of the interaction between inflammation and platelet activation, such as the toll-like receptors, myeloperoxidase, and platelet factor-4. The accumulating evidence is especially important in the era of the coronavirus disease-19 pandemic, characterized by an excessive inflammatory burden leading to thrombotic complications, partially mediated by platelet activation. Lastly, recent advances in anti-inflammatory therapies point towards an anti-thrombotic effect secondary to diminished platelet activation.

[24] *Leslie-Mazwi TM, Srivatanakul K*. **Coronavirus disease 2019 and stroke**. Interv Neuroradiol 2021; 27:13-18.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34670419
ABSTRACT
The multisystem nature of coronavirus disease 2019 has become increasingly clear over the course of the pandemic. Both the neurological and vascular systems are affected, impacting acute stroke. This impact can be conceptualised as direct and indirect effects of the disease. The direct effects of coronavirus disease 2019 on stroke are thought to relate to receptor-mediated tissue invasion and the marked inflammatory response to the presence of the virus. These effects include coagulopathies, endotheliitis, systemic inflammation and atherosclerotic plaque instability, with possibly long-term cardiovascular effects. The indirect effects impact all aspects of stroke care delivery. These extend far beyond the direct effects of coronavirus disease 2019, and represent an essential focus for stroke systems of care. In this article, we detail the impact of coronavirus disease 2019 on acute stroke.

[25] *Levy Y, Levy D*. **A Friend and a Foe: 50 Years of the Apolipoprotein E Research Trail**. The Israel Medical Association journal : IMAJ 2021; 23:665-669.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34672451
ABSTRACT

An arginine-rich apolipoprotein was discovered 50 years ago and became known as apolipoprotein E (ApoE) 10 years later. ApoE is associated with triglyceride-rich lipoproteins and mediates the clearance of these lipoproteins from the plasma. The ApoE-deficient hypercholesterolemic mice are an excellent platform for experimental atherosclerosis because they are similar to human pathology with regard to an atherogenic diet. ApoE is mainly produced in the liver and central nervous system cells. Three alleles determine six ApoE phenotypes with different metabolic effects and plasma cholesterol levels. Type III dysbetalipoproteinemia is associated with wide-spread atherogenesis with a defective ApoE2 resulting in delayed clearance of triglyceride-rich lipoproteins. ApoE4 substantially increases the risk including age of onset, progression, and prognosis of Alzheimer's disease. Therefore, much effort has been directed to the elucidation of the pathogenic role of ApoE related to amyloid β (Aβ) acquisition in the brain. The ApoE trail passing from an enigmatic protein to a major player in cardiovascular and neurodegenerative disorders is reviewed.

[26] *Itoga NK, Tawfik DS, Montez-Rath ME, Chang TI*. **Contributions of Systolic and Diastolic Blood Pressures to Cardiovascular Outcomes in the ALLHAT Study**. Journal of the American College of Cardiology 2021; 78:1671-1678.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34674811
ABSTRACT
BACKGROUND: SBP and DBP have important associations with cardiovascular events, but are seldom considered simultaneously. OBJECTIVES: This study sought to simultaneously analyze systolic blood pressure (SBP) and diastolic blood pressure (DBP) measurements on the associated risk of a primary composite outcome of all-cause mortality, myocardial infarction (MI), congestive heart failure (CHF), or stroke. METHODS: This study analyzed ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial) data, which randomized adults to chlorthalidone, amlodipine, or lisinopril. The authors evaluated the simultaneous association of repeated SBP and DBP measurements on the primary composite outcome, and each outcome using proportional hazards regression. The authors report hazard ratios using a "heat map" to represent high and low risk according to SBP and DBP combinations. RESULTS: During a median follow-up of 4.4 years (interquartile range: 3.6-5.4 years), 33,357 participants experienced 2,636 MIs, 866 CHF events, 936 strokes, and 3,700 deaths; 8,138 patients (24.4%) had at least 1 event. For the composite outcome, all-cause mortality, MI, and CHF, a U-shaped association was observed with SBP and DBP, but the SBP and DBP associated with the lowest hazards differed for each outcome. For example, SBP/DBP of 140-155/70-80 mm Hg was associated with the lowest HR for all-cause mortality, compared with 110-120/85-90 mm Hg for MI and 125-135/70-75 mm Hg for CHF. In contrast, the association of SBP and stroke was linear. CONCLUSIONS: The risk pattern of SBP and DBP differs by clinical outcomes, and the SBP and DBP associated with the lowest risk. Our results suggest individualization of blood pressure targets may depend in part on the cardiovascular event for which the patient is most at risk.

[27] *Vinciguerra M, Romiti S, Sangiorgi GM et al.* **SARS-CoV-2 and Atherosclerosis: Should COVID-19 Be Recognized as a New Predisposing Cardiovascular Risk Factor?** Journal of cardiovascular development and disease 2021; 8.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34677199
ABSTRACT

At the beginning of the COVID-19 pandemic, the lung was recognized as the main target organ; now, new evidence suggests that SARS-CoV-2 infection leads to vascular disease. In a previous review, we supposed a bidirectional link between endothelial dysfunction and COVID-19, identifying atherosclerosis as having a crucial role in its pathogenesis. Atherosclerosis with an existing endothelial dysfunction may worsen COVID-19 manifestations, leading to adverse outcomes, as largely reported. However, COVID-19 may be the trigger factor in the progression of the atherosclerotic process up to making it clinically manifest. The thrombotic complications can involve not only the atherosclerotic plaque, but also the durability of the surgical device implanted to treat a pre-existing coronary artery disease as recently reported. The burden of the disease makes necessary a long-term stratification of patients, revising drastically targeted therapy among others.

[28] *Aghasizadeh M, Nosrati M, Saberi-Karimian M et al.* **Association of ANGPTL3 polymorphisms with high-density lipoprotein cholesterol uptake capacity in patients with cardiovascular disease**. Journal of clinical laboratory analysis 2021; 35:e23980.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34689370

ABSTRACT

INTRODUCTION: Previous studies have shown the importance of angiopoietin-like 3 (ANGPTL3) as a modulator of lipid profiles. Cholesterol uptake capacity (CUC) is one means for assessing high-density lipoprotein (HDL) functionality. This study for the first time has investigated the relationship between genetic ANGPTL3 polymorphism and CUC in patients with cardiovascular disease. METHODS: Five hundred three subjects comprising 350 healthy subjects and 153 individuals who developed a cardiovascular disease (CVD) event during follow-up were recruited as part of the Mashhad Stroke and Heart Atherosclerotic Disorder (MASHAD) cohort study. A modified CUC method was used to determine the CUC of serum samples. Applied amplification refractory mutation system PCR was performed for ANGPTL3 variants genotyping including: rs10789117, rs1748195, and rs11207997. Sanger sequencing was applied to confirm the genotypes. RESULTS: The results showed that there was a significant relationship between the rs1748195 genotypes and HDL concentration in the CVD group ($p = 0.02$). Moreover, individuals with a GG genotype of the rs1748195 were associated with a lower risk of CVD (OR = 0.49, 95% CI = 0.24-0.98, $p = 0.04$) compared with CC genotype in the CUC ≤ 1.7 a.u subgroup. Moreover, the CT genotype of rs11207997 was associated with a lower risk of CVD (OR = 0.74, 95% CI = 0.41-1.3, $p = 0.01$) compared with CC genotype in CUC > 1.7 a.u subgroup. CONCLUSION: The results showed that the CT genotype of the rs11207997 variant was associated with a lower risk of incident CVD in patients with higher HDL functionality. As well, the rs1748195 gene variant may contribute to a reduced risk of CVD.

[29] *Li X, Chen B, Zhou X et al.* **Identification of dyslipidemia as a risk factor for sudden sensorineural hearing loss: A multicenter case-control study**. Journal of clinical laboratory analysis 2021; 35:e24067.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34674306

ABSTRACT

BACKGROUND: Recently, several studies have reported an association between lipid profiles and sudden sensorineural hearing loss (SSNHL), yet there is considerable variability between the individual studies in defining the precise association between serum lipids levels and SSNHL. This

study sought to identify a possible relationship between dyslipidemia and the prevalence and prognosis of SSNHL. METHODS: A case-control study was carried out at two independent medical centers, including 2,288 SSNHL patients and 2,288 healthy controls. Clinical characteristics and serum lipid parameters were assessed, including total cholesterol (CHOL), high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides (Trig), apolipoprotein AI (ApoAI), apolipoprotein B (ApoB), and lipoprotein a (Lpa). Multivariate logistic regression analysis was performed to assess the relationship between lipid profiles and SSNHL in the 4,576 subjects. RESULTS: Significant differences were identified in several conventional serum lipid markers including CHOL, Trig, HDL, LDL, ApoAI, ApoB, and Lpa, between SSNHL patients and healthy controls. Serum ApoAI levels were significantly lower in patients with bilateral SSNHL compared to unilateral SSNHL. Binary logistic regression analysis revealed that higher levels of ApoB, LDL, Trig, and lower levels of ApoAI and HDL were all associated with an increased risk of SSNHL. After clinical characterization, multivariate analysis showed that only low levels of ApoB predicted likelihood of a recovery of more than 30 dB among patients with SSNHL. CONCLUSIONS: Serum lipids are associated with the incidence and prognosis of SSNHL. Identification of dyslipidemia may improve early evaluation and management of SSNHL risks.

[30] *Calabria S, Ronconi G, Dondi L et al.* **Coronary Artery Disease in Patients Older than 35 and Eligible for Cardiovascular Secondary Prevention: An Italian Retrospective Observational Analysis of Healthcare Administrative Databases**. Journal of clinical medicine 2021; 10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34682831
ABSTRACT
BACKGROUND: This study describes patients with coronary artery disease (CAD) who are eligible for secondary prevention and assesses their healthcare consumption and costs from the perspective of the Italian National Health Service (INHS). METHODS: From the Fondazione Ricerca e Salute's database, which collects Italian healthcare administrative data, all patients aged ≥ 35, with ≥1 primary in-hospital CAD diagnosis and/or procedure on the coronary arteries, or with the specific disease exemption code, and who are suitable for long-term secondary prevention treatments, were identified in 2018 and analyzed. Demographics, comorbidities, one-year supplied drugs, hospitalizations, and costs were analyzed. RESULTS: From >3 million inhabitants aged ≥ 35, 46,063 (1.3%) were identified (72.1% males, mean age 70 ± 12; approximately 50% with ≥3 comorbidities). During a one-year follow-up, 96.4% were treated with ≥1 drug for secondary prevention (mainly antiplatelets and lipid lowering agents), 69.4% with ≥1 concomitant cardiovascular drug, and 95.8% with ≥1 concomitant non-cardiovascular therapy. Within one year, 30.6% of patients were hospitalized at least once, mostly due to non-cardiovascular events. Calculated by mean, the INHS paid EUR 6078 per patient. CONCLUSIONS: This analysis confirms the relevant burden of CAD for patients with many comorbidities and who are frequently hospitalized, and the burden on the INHS. A multidisciplinary healthcare approach is encouraged to improve patients' outcomes and reduce costs for the INHS.

[31] *Muñoz-Gómez A, Fernández-Cruz A, Lavilla-Olleros C et al.* **Real-Life Impact of Glucocorticoid Treatment in COVID-19 Mortality: A Multicenter Retrospective Study**. Journal of clinical medicine 2021; 10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34682801

ABSTRACT
We aimed to determine the impact of steroid use in COVID-19 in-hospital mortality, in a retrospective cohort study of the SEMICOVID19 database of admitted patients with SARS-CoV-2 laboratory-confirmed pneumonia from 131 Spanish hospitals. Patients treated with corticosteroids were compared to patients not treated with corticosteroids; and adjusted using a propensity-score for steroid treatment. From March-July 2020, 5.262 (35.26%) were treated with corticosteroids and 9.659 (64.73%) were not. In-hospital mortality overall was 20.50%; it was higher in patients treated with corticosteroids than in controls (28.5% versus 16.2%, OR 2.068 [95% confidence interval; 1.908 to 2.242]; p = 0.0001); however, when adjusting by occurrence of ARDS, mortality was significantly lower in the steroid group (43.4% versus 57.6%; OR 0.564 [95% confidence interval; 0.503 to 0.633]; p = 0.0001). Moreover, the greater the respiratory failure, the greater the impact on mortality of the steroid treatment. When adjusting these results including the propensity score as a covariate, in-hospital mortality remained significantly lower in the steroid group (OR 0.774 [0.660 to 0.907], p = 0.002). Steroid treatment reduced mortality by 24% relative to no steroid treatment (RRR 0.24). These results support the use of glucocorticoids in COVID-19 in this subgroup of patients.

[32] *Ozuynuk AS, Erkan AF, Dogan N et al.* **Examining the effects of the CLU and APOE polymorphisms' combination on coronary artery disease complexed with type 2 diabetes mellitus**. Journal of diabetes and its complications 2021:108078.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34686405

ABSTRACT
AIMS: Coronary artery disease (CAD) and type 2 diabetes mellitus (T2DM) are important and increasing public health problems. This study aimed to identify the impact of APOE and CLU gene polymorphisms on the prevalence of both diseases, along with the effect of these polymorphisms on lipid profile and glucose metabolism. METHODS: 736 CAD patients (≥50 stenosis) and 549 non-CAD subjects (≤30 stenosis) were genotyped for APOE (rs429358 and rs7412) and CLU (rs11136000) gene polymorphisms using hydrolysis probes in real-time PCR. Blood samples of the individuals were drawn before coronary angiography and biochemical analyses were done. The associations between the polymorphisms and the selected parameters were assessed using statistical analysis. RESULTS: In this study, the ε2 and ε4 isoforms of apoE were associated with serum lipid levels and TC/HDL-C and LDL-C/HDL-C ratios in analysis adjusted for several confounders and in crude analysis. It was observed that CLU T allele carrier non-CAD subjects had lower glycosylated hemoglobin levels. Furthermore, the effects of APOE and CLU polymorphisms were assessed on CAD and T2DM presence. In crude and multiple logistic regression analyses, the ε2 isoform carriers had a lower risk for CAD complexed with T2DM. When the combinational effects of APOE and CLU polymorphisms were examined, the ε2 and T allele carriers had decreased risk for CAD complexed with T2DM compared to non-carriers. CONCLUSIONS: In conclusion, the combination of APOE and CLU polymorphisms is associated with CAD-DM status along with the APOE ε2 isoform by itself, and the apoE isoforms are strongly associated with serum lipid levels.

[33] *Hirano T, Satoh N, Kodera R et al.* **Dyslipidemia in diabetic kidney disease classified by proteinuria and renal dysfunction: A cross-sectional study from a regional diabetes cohort**. Journal of diabetes investigation 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34665936

ABSTRACT
AIMS/INTRODUCTION: Diabetic kidney disease (DKD) exacerbates dyslipidemia and increases the incidence of atherosclerotic cardiovascular disease. DKD is a concept that includes typical diabetic nephropathy and an atypical phenotype without proteinuria. We investigated dyslipidemia in different DKD phenotypes that have not been fully studied. MATERIALS AND METHODS: Fasting plasma was obtained from 1,073 diabetes patients enrolled in the regional diabetes cohort (ViNA cohort). Non-proteinuric and proteinuric DKD were defined as an estimated glomerular filtration rate <60 mL/min/1.73 m(2) in the absence or presence of urinary albumin-to-creatinine ratio >300 mg/g. Novel lipid risk factors, low-density lipoprotein (LDL) triglyceride (TG) and small dense LDL cholesterol were measured using our established homologous assay. RESULTS: The proportion of atherosclerotic cardiovascular disease patients was higher in non-proteinuric DKD and even higher in proteinuric DKD than in non-DKD. Increased estimated glomerular filtration rate grade and albuminuric stage were independently correlated with higher TG, TG-rich lipoprotein cholesterol and apolipoprotein CIII. Therefore, proteinuric DKD had the highest of these levels. Small dense LDL cholesterol and LDL-TG were higher in the proteinuria without renal dysfunction group in the lipid-lowering drug-free subset. Lipoprotein(a) was higher in DKD regardless of proteinuria. CONCLUSIONS: Proteinuria was associated with an atherogenic subspecies of LDL, whereas renal dysfunction was associated with increased lipoprotein(a). Proteinuria and renal dysfunction independently exacerbated TG-rich lipoprotein-related dyslipidemia. This is in good agreement with the results of large-scale clinical studies in which proteinuria and renal dysfunction synergistically increased the risk of atherosclerotic cardiovascular disease in populations with diabetes.

[34] *Kondakov A, Lelyuk V*. **Clinical Molecular Imaging for Atherosclerotic Plaque**. J Imaging 2021; 7.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34677297
ABSTRACT
Atherosclerosis is a well-known disease leading to cardiovascular events, including myocardial infarction and ischemic stroke. These conditions lead to a high mortality rate, which explains the interest in their prevention, early detection, and treatment. Molecular imaging is able to shed light on the basic pathophysiological processes, such as inflammation, that cause the progression and instability of plaque. The most common radiotracers used in clinical practice can detect increased energy metabolism (FDG), macrophage number (somatostatin receptor imaging), the intensity of cell proliferation in the area (labeled choline), and microcalcifications (fluoride imaging). These radiopharmaceuticals, especially FDG and labeled sodium fluoride, can predict cardiovascular events. The limitations of molecular imaging in atherosclerosis include low uptake of highly specific tracers, possible overlap with other diseases of the vessel wall, and specific features of certain tracers' physiological distribution. A common protocol for patient preparation, data acquisition, and quantification is needed in the area of atherosclerosis imaging research.

[35] *Futema M, Taylor-Beadling A, Williams M, Humphries SE*. **Genetic testing for Familial Hypercholesterolaemia - Past, Present and Future**. Journal of lipid research 2021; 62:100139.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34666015
ABSTRACT

In the early 1980s, the Nobel Prize winning cellular and molecular work of Mike Brown and Joe Goldstein led to the identification of the Low Density Lipoprotein Receptor (LDLR) gene as the first gene where mutations cause the Familial Hypercholesterolaemia (FH) phenotype. We now know that autosomal dominant monogenic FH can be caused by pathogenic variants of three additional genes (APOB/PCSK9/APOE), and that the plasma LDL-C concentration and risk of premature Coronary Heart Disease (CHD) differs according to the specific locus and associated molecular cause. It is now possible to use Next Generation Sequencing (NGS) to sequence all exons of all four genes, processing 96 patient samples in one sequencing run, increasing the speed of test results and reducing costs. This has resulted in the identification of many novel FH-causing variants, but also some "Variants of Unknown Significance (VUSs)" which require further evidence to classify as pathogenic or benign. The identification of the FH-causing variant in an index case can be used as an unambiguous and rapid test for other family members. An FH-causing variant can be found in 20%-40% of patients with the FH phenotype, and we now appreciate that in the majority of patients without a monogenic cause, a polygenic aetiology for their phenotype is highly likely. Compared to those with a monogenic cause, these patients have significantly lower risk of future CHD. The use of these molecular genetic diagnostic methods in the characterization of FH is a prime example of the utility of precision or personalised medicine.

[36] *Ottun AT, Odunsi MA, Jinadu FO et al.* **Maternal hyperlipidemia and spontaneous preterm delivery: a multi-centre cohort study**. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet 2021:1-6.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34662530

ABSTRACT

BACKGROUND: Hyperlipidemia is a precursor of inflammation and oxidative stress and suggested to be associated with adverse pregnancy outcomes such as preterm delivery. This study evaluated the association between maternal hyperlipidemia and spontaneous preterm delivery. METHODS: This was a prospective, multicentre cohort study in which 239 pregnant women aged 20-35 years with singleton pregnancy, were consecutively recruited at estimated gestational ages of 14-18weeks. Maternal serum lipids were determined at recruitment over a 2-month period and they were followed up until 37 weeks for the subsequent 6 months. Pregnant women with medical conditions and medications that could alter serum lipid levels were excluded from the study. Demographic and baseline variables were summarized using descriptive statistics. Comparison of continuous variables was done using the student's t-test and categorical variables were compared using the Chi square or Fisher's exact test as appropriate. Correlation was determined using Pearson's correlation. Odd ratios were calculated at 95% confidence interval, width of CI as 10% (0.1) and all significances are reported at $p < .05$. FINDINGS: The prevalence of spontaneous preterm delivery and maternal hypercholesterolemia was 10.2% and 33.1% respectively. There was no significant association between spontaneous preterm delivery and hyperlipidemia in pregnancy ($p = .102$). Mean serum total cholesterol (mmol/L), LDL cholesterol (mmol/L), HDL cholesterol (mmol/L) and triglyceride (mmol/L) was 5.31 ± 0.84, 2.60 ± 0.72, 1.64 ± 0.36 and 1.23 ± 0.40 respectively in women with spontaneous preterm delivery was similar to mean values of 5.23 ± 0.98, 2.54 ± 0.82, 1.64 ± 0.49 and 1.30 ± 0.59 respectively in women with term delivery. There was no significant correlation between mean individual serum lipids, determined at 14-18weeks gestational age, and gestational age at delivery.

CONCLUSION: Serum lipid values determined early in pregnancy were observed to be similar in women with preterm and term delivery. There was no association between hyperlipidemia and spontaneous preterm delivery. There was no correlation of individual mean lipid values, determined early in pregnancy, and gestational age at delivery.

[37] *Tünnemann-Tarr A, Scharnagl H, Katzmann JL et al.* **Familial chylomicronemia syndrome due to a heterozygous deletion of the chromosome 8 treated with the apoCIII inhibitor volanesorsen: A case report**. Medicine (Baltimore) 2021; 100:e27573.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34678899
ABSTRACT
RATIONALE: Familial chylomicronemia syndrome is a congenital, severe form of hypertriglyceridemia associated with increased risk of acute pancreatitis. Treatment options are limited. PATIENT CONCERNS: A 52-year-old woman was referred with recurrent pancreatitis and severe hypertriglyceridemia to our lipid clinic. DIAGNOSIS: Laboratory examination showed elevated serum triglyceride concentrations of 8090 mg/dL (90 mmol/L). Lipid electrophoresis showed a type V phenotype with positive chylomicrons. Genetic investigation revealed a novel heterozygous large deletion of the lipoprotein lipase gene on chromosome 8. A familial chylomicronemia syndrome was diagnosed. Other causes of hypertriglyceridemia were excluded. INTERVENTIONS: Fibrates and diet did not lower triglyceride levels. Therefore, treatment with the apolipoprotein CIII (apoCIII) inhibitor volanesorsen was initiated. OUTCOMES: After 3 months of treatment, a 90% reduction of triglycerides was observed. ApoCIII concentrations were reduced by 90% in the total and by 61% in the chylomicron-free serum. Treatment was well tolerated with only minor local reaction after the first application. The platelet count was monitored weekly and did not decrease <150 cells/μL. LESSONS: This case report shows that inhibition of apoCIII potently reduces serum triglycerides in patients with heterozygous monogenetic deletion of the lipoprotein lipase gene. Follow-up will show the effect on recurrent episodes of pancreatitis.

[38] *Wu G, Ji Q, Huang H, Zhu X*. **The efficacy of fish oil in preventing coronary heart disease: A systematic review and meta-analysis**. Medicine (Baltimore) 2021; 100:e27253.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34664872
ABSTRACT
BACKGROUND: Coronary heart disease (CHD) is one of the most common causes of death and disease burden in the world. Current fish oil aiming to prevent and treat CHD have shown a large variety of effects with low levels of evidence. OBJECTIVE: To evaluate the efficacy of fish oil for protection against CHD, we conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) evaluating the use of fish oil for protection against CHD. METHODS: We retrieved relevant articles published from January 1966 to January 2020 by searching the PubMed, EMBASE, Cochrane CENTRAL, and Web of Science databases. RCTs of fish oil in preventing CHD were selected. The study quality was evaluated using the Cochrane Risk of Bias tool with RevMan 5.3 software. The first selection involved 360 citations. After screening and evaluation of suitability, 19 RCTs adjusted for clustering were included in the meta-analysis. All selected manuscripts considered that fish oil was effective in preventing CHD, secondary outcome measures included angina, sepsis and death. RESULTS: Compared with the control group, fish oil may confer significant protection against CHD (odds ratio=0.84; 95% confidence interval: 0.72-0.98). There was no significant

difference in the incidence of secondary outcomes between the observation group and the control group (P>.05). CONCLUSION: The above results show that fish oil plays an important role in reducing CHD and cardiovascular events. However, because of the suboptimal quality of the studies included into the meta-analysis, these results do not justify adding fish oils systematically to the heavy pharmaceutical assortment already recommended in CHD patients. REGISTRATION DETAILS: CRD42020183719.

[39] *Behbodikhah J, Ahmed S, Elyasi A et al.* **Apolipoprotein B and Cardiovascular Disease: Biomarker and Potential Therapeutic Target**. Metabolites 2021; 11.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34677405
ABSTRACT
Apolipoprotein (apo) B, the critical structural protein of the atherogenic lipoproteins, has two major isoforms: apoB48 and apoB100. ApoB48 is found in chylomicrons and chylomicron remnants with one apoB48 molecule per chylomicron particle. Similarly, a single apoB100 molecule is contained per particle of very-low-density lipoprotein (VLDL), intermediate density lipoprotein, LDL and lipoprotein(a). This unique one apoB per particle ratio makes plasma apoB concentration a direct measure of the number of circulating atherogenic lipoproteins. ApoB levels indicate the atherogenic particle concentration independent of the particle cholesterol content, which is variable. While LDL, the major cholesterol-carrying serum lipoprotein, is the primary therapeutic target for management and prevention of atherosclerotic cardiovascular disease, there is strong evidence that apoB is a more accurate indicator of cardiovascular risk than either total cholesterol or LDL cholesterol. This review examines multiple aspects of apoB structure and function, with a focus on the controversy over use of apoB as a therapeutic target in clinical practice. Ongoing coronary artery disease residual risk, despite lipid-lowering treatment, has left patients and clinicians with unsatisfactory options for monitoring cardiovascular health. At the present time, the substitution of apoB for LDL-C in cardiovascular disease prevention guidelines has been deemed unjustified, but discussions continue.

[40] *Gordillo-Marañón M, Zwierzyna M, Charoen P et al.* **Validation of lipid-related therapeutic targets for coronary heart disease prevention using human genetics**. Nature communications 2021; 12:6120.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34675202
ABSTRACT
Drug target Mendelian randomization (MR) studies use DNA sequence variants in or near a gene encoding a drug target, that alter the target's expression or function, as a tool to anticipate the effect of drug action on the same target. Here we apply MR to prioritize drug targets for their causal relevance for coronary heart disease (CHD). The targets are further prioritized using independent replication, co-localization, protein expression profiles and data from the British National Formulary and clinicaltrials.gov. Out of the 341 drug targets identified through their association with blood lipids (HDL-C, LDL-C and triglycerides), we robustly prioritize 30 targets that might elicit beneficial effects in the prevention or treatment of CHD, including NPC1L1 and PCSK9, the targets of drugs used in CHD prevention. We discuss how this approach can be generalized to other targets, disease biomarkers and endpoints to help prioritize and validate targets during the drug development process.

[41] *Rifai MA, Ballantyne CM*. **PCSK9-targeted therapies: present and future approaches**. Nature reviews. Cardiology 2021; 18:805-806.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34663945
ABSTRACT

[42] *Ahrens AP, Culpepper T, Saldivar B et al.* **A Six-Day, Lifestyle-Based Immersion Program Mitigates Cardiovascular Risk Factors and Induces Shifts in Gut Microbiota, Specifically Lachnospiraceae, Ruminococcaceae, Faecalibacterium prausnitzii: A Pilot Study**. Nutrients 2021; 13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34684459
ABSTRACT
Cardiovascular disease (CVD) prevalence remains elevated globally. We have previously shown that a one-week lifestyle "immersion program" leads to clinical improvements and sustained improvements in quality of life in moderate to high atherosclerotic CVD (ASCVD) risk individuals. In a subsequent year of this similarly modeled immersion program, we again collected markers of cardiovascular health and, additionally, evaluated intestinal microbiome composition. ASCVD risk volunteers (n = 73) completed the one-week "immersion program" involving nutrition (100% plant-based foods), stress management education, and exercise. Anthropometric measurements and CVD risk factors were compared at baseline and post intervention. A subgroup (n = 22) provided stool, which we analyzed with 16S rRNA sequencing. We assessed abundance changes within-person, correlated the abundance shifts with clinical changes, and inferred functional pathways using PICRUSt. Reductions in blood pressure, total cholesterol, and triglycerides, were observed without reduction in weight. Significant increases in butyrate producers were detected, including Lachnospiraceae and Oscillospirales. Within-person, significant shifts in relative abundance (RA) occurred, e.g., increased Lachnospiraceae (+58.8% RA, p = 0.0002), Ruminococcaceae (+82.1%, p = 0.0003), Faecalibacterium prausnitzii (+54.5%, p = 0.002), and diversification and richness. Microbiota changes significantly correlated with body mass index (BMI), blood pressure (BP), cholesterol, high-sensitivity C-reactive protein (hsCRP), glucose, and trimethylamine N-oxide (TMAO) changes. Pairwise decreases were inferred in microbial genes corresponding to cancer, metabolic disease, and amino acid metabolism. This brief lifestyle-based intervention improved lipids and BP and enhanced known butyrate producers, without significant weight loss. These results demonstrate a promising non-pharmacological preventative strategy for improving cardiovascular health.

[43] *Borsche L, Glauner B, von Mendel J*. **COVID-19 Mortality Risk Correlates Inversely with Vitamin D3 Status, and a Mortality Rate Close to Zero Could Theoretically Be Achieved at 50 ng/mL 25(OH)D3: Results of a Systematic Review and Meta-Analysis**. Nutrients 2021; 13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34684596
ABSTRACT
BACKGROUND: Much research shows that blood calcidiol (25(OH)D3) levels correlate strongly with SARS-CoV-2 infection severity. There is open discussion regarding whether low D3 is caused by the infection or if deficiency negatively affects immune defense. The aim of this study was to collect further evidence on this topic. METHODS: Systematic literature search was performed to identify retrospective cohort as well as clinical studies on COVID-19 mortality rates versus D3 blood levels. Mortality rates from clinical studies were corrected for age, sex, and diabetes. Data were analyzed

using correlation and linear regression. RESULTS: One population study and seven clinical studies were identified, which reported D3 blood levels preinfection or on the day of hospital admission. The two independent datasets showed a negative Pearson correlation of D3 levels and mortality risk ($r(17) = -0.4154$, $p = 0.0770$/$r(13) = -0.4886$, $p = 0.0646$). For the combined data, median (IQR) D3 levels were 23.2 ng/mL (17.4-26.8), and a significant Pearson correlation was observed ($r(32) = -0.3989$, $p = 0.0194$). Regression suggested a theoretical point of zero mortality at approximately 50 ng/mL D3. CONCLUSIONS: The datasets provide strong evidence that low D3 is a predictor rather than just a side effect of the infection. Despite ongoing vaccinations, we recommend raising serum 25(OH)D levels to above 50 ng/mL to prevent or mitigate new outbreaks due to escape mutations or decreasing antibody activity.

[44] *Herrera Vielma F, Valenzuela R, Videla LA, Zúñiga-Hernández J.* **N-3 Polyunsaturated Fatty Acids and Their Lipid Mediators as A Potential Immune-Nutritional Intervention: A Molecular and Clinical View in Hepatic Disease and Other Non-Communicable Illnesses**. Nutrients 2021; 13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34684386
ABSTRACT
In recent years, the beneficial effect of n-3 polyunsaturated fatty acids (n-3 PUFAs) intake on human health has been widely accepted in the field of immunonutrition. Today, we find a diversity of supplements based on n-3 PUFAs and/or minerals, vitamins and other substances. The main objective of this review is to discuss the importance of n-3 PUFAs and their derivatives on immunity and inflammatory status related to liver disease and other non-communicable illnesses. Based on the burden of liver diseases in 2019, more than two million people die from liver pathologies per year worldwide, because it is the organ most exposed to agents such as viruses, toxins and medications. Consequently, research conducted on n-3 PUFAs for liver disease has been gaining prominence with encouraging results, given that these fatty acids have anti-inflammatory and cytoprotective effects. In addition, it has been described that n-3 PUFAs are converted into a novel species of lipid intermediaries, specialized pro-resolving mediators (SPMs). At specific levels, SPMs improve the termination of inflammation as well as the repairing and regeneration of tissues, but they are deregulated in liver disease. Since evidence is still insufficient to carry out pharmacological trials to benefit the resolution of acute inflammation in non-communicable diseases, there remains a call for continuing preclinical and clinical research to better understand SPM actions and outcomes.

[45] *Song P, Man Q, Li Y et al.* **Association between Dietary Patterns and Low HDL-C among Community-Dwelling Elders in North China**. Nutrients 2021; 13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34684309
ABSTRACT
We aimed to investigate the association between dietary patterns and low HDL-C among the elderly population living in North China. The data were from a national cross-sectional survey conducted in 2015. General information in terms of living habits, health status, and food intake using 24 h dietary recall for three consecutive days was procured, and the weight of edible oil and condiments recorded. Anthropometric index, blood pressure, and fasting serum lipids were measured using standard methods. Dietary patterns were derived from food categories by exploratory factor analysis, and multivariate logistic regression was used to estimate the odds ratios of low HDL-C across quartiles of

dietary patterns. Among 3387 elderly participants, 21.9% had low HDL-C levels. After adjusting for potential confounding factors, participants with highest score versus lowest score in the balanced dietary pattern had a decreased risk of low HDL-C (OR = 0.38, 95% CI: 0.16-0.88, p for trend = 0.013) in the group with a BMI of 27.1 kg/m(2) and above. Compared to the lowest quartile, there was a statistically significant negative association between the highest scores of the Western dietary pattern and low HDL-C (OR = 0.37, 95% CI: 0.17-0.82, p for trend = 0.018) in the group with a BMI of 21.6-24.8 kg/m(2). However, greater adherence to a thrifty dietary pattern (highest quartiles vs. lowest quartiles) was associated with increased risk of low HDL-C (OR = 3.31, 95% CI: 1.05-10.40, p for trend = 0.044), especially in the subgroup with a BMI of 21.6 kg/m(2) and below. The study revealed that it is urgent to develop district-specific dietary improvement plans for dyslipidemia based on the nutritional status of the elderly population in North China.

[46] *Williams KA, Fughhi I, Fugar S et al.* **Nutrition Intervention for Reduction of Cardiovascular Risk in African Americans Using the 2019 American College of Cardiology/American Heart Association Primary Prevention Guidelines**. Nutrients 2021; 13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34684423

ABSTRACT

INTRODUCTION: The 2019 American College of Cardiology/American Heart Association (ACC/AHA) Prevention Guidelines emphasize reduction in dietary sodium, cholesterol, refined carbohydrates, saturated fat and sweetened beverages. We hypothesized that implementing this dietary pattern could reduce cardiovascular risk in a cohort of volunteers in an urban African American (AA) community church, during a 5-week ACC/AHA-styled nutrition intervention, assessed by measuring risk markers and adherence, called HEART-LENS (Helping Everyone Assess Risk Today Lenten Nutrition Study). METHODS: The study population consisted of 53 volunteers who committed to eat only home-delivered non-dairy vegetarian meals (average daily calories 1155, sodium 1285 mg, cholesterol 0 mg; 58% carbohydrate, 17% protein, 25% fat). Body mass index (BMI) and fasting serum markers of cardiometabolic and risk factors were measured, with collection of any dietary deviation. RESULTS: Of 53 volunteers, 44 (mean age 60.2 years, 37 women) completed the trial (88%); 1 was intolerant of the meals, 1 completed both blood draws but did not eat delivered food, and 7 did not return for the tests. Adherence to the diet was reported at 93% in the remaining 44. Cardiometabolic risk factors improved significantly, highlighted by a marked reduction in serum insulin (-43%, p = 0.000), hemoglobin A1c (6.2% to 6.0%, p = 0.000), weight and BMI (-10.2 lbs, 33 to 31 kg/m(2), p = 0.000), but with small reductions of fasting glucose (-6%, p = 0.405) and triglyceride levels (-4%, p = 0.408). Additionally, improved were trimethylamine-N-oxide (5.1 to 2.9 μmol/L, -43%, p = 0.001), small dense low-density lipoprotein cholesterol (LDL) (24.2 to 19.1 mg/dL, -21%, p = 0.000), LDL (121 to 104 mg/dL, -14%, p = 0.000), total cholesterol (TC) (190 to 168 mg/dL, -12%, p = 0.000), and lipoprotein (a) (LP(a)) (56 to 51 mg/dL, -11%, p = 0.000); high sensitivity C-reactive protein (hs-CRP) was widely variable but reduced by 16% (2.5 to 2.1 ng/mL, p = NS) in 40 subjects without inflammatory conditions. Soluble urokinase plasminogen activator (suPAR) levels were not significantly changed. The ACC/AHA pooled cohort atherosclerotic cardiovascular disease (ASCVD) risk scores were calculated for 41 and 36 volunteers, respectively, as the ASCVD risk could not be calculated for 3 subjects with low lipid fractions at baseline and 8 subjects after intervention (p = 0.184). In the remaining subjects, the mean 10-year risk was reduced from 10.8 to 8.7%, a 19.4% decrease (p = 0.006), primarily due to a 14% decrease in low-density lipoprotein cholesterol and a 10

mm Hg (6%) reduction in systolic blood pressure. CONCLUSIONS: In this prospective 5-week non-dairy vegetarian nutrition intervention with good adherence consistent with the 2019 ACC/AHA Guidelines in an at-risk AA population, markers of cardiovascular risk, cardiometabolism, and body weight were significantly reduced, including obesity, low-density lipoprotein cholesterol (LDLc) density, LP(a), inflammation, and ingestion of substrates mediating production of trimethylamine-N-oxide (TMAO). Albeit reduced, hs-CRP and suPAR, were not lowered consistently. This induced a significant decrease in the 10-year ASCVD risk in this AA cohort. If widely adopted, this could dramatically reduce and possibly eradicate, the racial disparity in ASCVD events and mortality, if 19% of the 21% increase is eliminated by this lifestyle change.

[47] *Barman HA, Pala AS, Dogan O et al.* **Prognostic significance of temporal changes of lipid profile in COVID-19 patients**. Obes Med 2021; 28:100373.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34671707
ABSTRACT
BACKGROUND: COVID-19 is a multisystemic disease that affects many organs and has metabolic effects. AIMS: This study aims to investigate the effect of the temporal changes of lipid levels on the prognosis during the course of the disease. STUDY DESIGN: Retrospective cross-sectional study. METHODS: For this single-center study, data of patients who were treated for COVID-19 were collected. Fasting lipid parameters including total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride (TG) levels were collected within 24 h of hospitalization. For investigation of temoral changes in lipid parameters, the results of the same parameters in the one-year period before COVID-19 were collected from medical records. A total number of 324 eligible COVID-19 patients were included in this study. The association of changes of lipid parameters with COVID-19 symptom severity and in-hospital mortality were investigated. RESULTS: The mean age of the severe group (n = 139) was 65.4 ± 15.5 years, and 60% were male. TC, LDL-C and HDL-C levels were significantly lower compared to pre-COVID measurements in the study population. Multiple linear regression analysis determined age, acute kidney injury, hs-Troponin, D-dimer, temporal changes in TC, and TG levels were determined as independent predictors for the development of COVID-19 mortality. CONCLUSION: Our findings showed that temporal changes in lipid parameters before and after COVID-19 may be associated with mortality and in-hospital adverse outcomes.

[48] *Dimény E, Bán E, Fekete LG, Brassai A*. **[Low cholesterol level as a possible suicide risk factor]**. Orvosi hetilap 2021; 162:1732-1739.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34689130
ABSTRACT
Összefoglaló. Bevezetés: A koleszterinszint a köztudatban elsősorban mint cardiovascularis rizikófaktor van jelen. Nem mellékes azonban, hogy akár a magas, akár az alacsony koleszterinszint direkt összefüggésbe hozható számos pszichiátriai kórképpel. Célkitűzés: A jelen tanulmány célja felhívni a figyelmet a holisztikus nézőpont kialakítására, hisz a hypercholesterinaemia korai cardiovascularis elhalálozáshoz vezethet, viszont alacsony koleszterinszint esetén megnövekedhet a hangulatzavarra és főleg az öngyilkosságra való hajlam. Módszer: Kutatásunkban 200 olyan pszichiátriai beteg összkoleszterinszintjét vizsgáltuk meg, akik öngyilkossági gondolatokkal küszködtek. Az öngyilkossági veszélyt a Modified Scale for Suicide Ideation (Miller és mtsai)

segítségével mértük. Eredmények: Az elért pontszámok alapján 3 kategóriába soroltuk a betegeket: 52 minimális suicid késztetésű, 49 középsúlyos és 99 súlyos rizikójú beteg. A legsúlyosabb kategóriába tartozó betegek nagy többségének (83 páciens, 84%) összkoleszterinje 4,5 mmol/l alatti volt. A másik két kategóriában ezen arány jelentősen kisebbnek bizonyult: a minimális suicid késztetésű kategóriában ez az érték csak 3 betegre (6%) volt vonatkoztatható, és a középsúlyosak esetén is csak 13 betegre (29%). Megbeszélés: Ezen tanulmányunk hátrányát képezheti a relatíve kis betegszám és a longitudinális utánkövetés megvalósításának hiánya. Következtetés: Jelen eredményeink alapján jogosan vetődhet fel a koleszterinszint mérésének rutinszerű bevezetése mint hatásos, szűrésre alkalmas öngyilkossági rizikófaktor biomarker. Orv Hetil. 2021; 162(43): 1732-1739. INTRODUCTION: High cholesterol levels are widely recognized as cardiovascular risk factors. However, lower or higher cholesterol levels can be in a solid relationship with several mental disorders, too. OBJECTIVE: Our study aims to raise awareness about the fact that hypocholesterolemia is involved in various mood disorders and even suicidal behavior looks to be much more frequent. METHOD: Our current study implicates 200 psychiatric patients. These subjects had suicidal ideation upon hospital referral. In the first 24 hours, their total cholesterol levels were measured and the severity of self-harm intentions was evaluated with the Modified Scale for Suicide Ideation by Miller et al. Results: By the obtained evaluation score we differentiated 3 groups: 52 patients with low suicide risk, 49 with moderate risk and 99 with high suicide risk. In this last group, 83 patients had their serum total cholesterol level under 4,5 mmol/L (84%). By comparison, in the low-risk category only 3 patients (6%) and in the moderate-risk 13 patients (29%) were with such levels. DISCUSSION: Clear conclusion cannot be drawn due to the reduced number of our patients, due to the absence of long-term consequent monitorization, and due to the heterogeneity of the studied population. CONCLUSION: Considering these data, a possible usefulness of total cholesterol levels in psychiatric patients may be suggested as a screening tool for the severity of suicidal ideation. Orv Hetil. 2021; 162(43): 1732-1739.

[49] *Favela-Mendoza AF, Rodríguez-Rodríguez BG, Rojas-Prado E et al.* **Prevalence of protective haplotypes of the SLCO1B1 gene for statin transport in Mexican populations**. Personalized medicine 2021; 18:533-540.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34674552

ABSTRACT

Aim: To evaluate the genetic distribution of the rs4149056 and rs2306283 variants in the SLCO1B1 gene in Mexican Mestizo (admixed) and Native American groups. Materials & methods: We recruited 360 volunteers who were qPCR-genotyped with TaqMan probes. Results: Allele and genotype frequencies are reported. Among the expected rs4149056-rs2306283 haplotypes, T-A (42.35-58.47%) was the most prevalent which relates to the normal activity of the OATP1B1 transporter. This was followed by the T-G haplotype associated with further statin transport and cholesterol reduction (32.49-43.76%). Conclusion: Based on these SLCO1B1 gene variants, we confirmed that a minimum fraction of the Mexican study populations would be at risk from decreasing simvastatin transport and the development of statin-induced myopathy.
Lay abstract The clinical response to statins, mainly atorvastatin and simvastatin, can be modified by interindividual variability including variations in the SLCO1B1 gene. This gene, that encodes the statin transporter OATP1B1, helps to regulate the cholesterol levels in the blood and is responsible for the presence of adverse drug reactions related to the statin consumption, such as muscular sickness.

This study analyzes the distribution of the SLCO1B1 gene variants rs4149056 and rs2306283 in geographically dispersed samples of the two main populations in Mexico: two Mestizo (admixed) populations and three Native American groups. We found that the genetic combinations of T–A and T–G for the two SLCO1B1 gene variants – associated with normal or efficient activity of the transporter OATP1B – were predominant in all of the study population. Therefore, the SLCO1B1 gene variability suggests that a majority of the Mexican population will respond favorably to simvastatin and have a low risk of developing associated muscular complications.
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[50] *Kim JB, Song WH, Park JS et al.* **Correction: A randomized, open-label, parallel, multi-center Phase IV study to compare the efficacy and safety of atorvastatin 10 and 20 mg in high-risk Asian patients with hypercholesterolemia**. PloS one 2021; 16:e0259072.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34669740
ABSTRACT
[This corrects the article DOI: 10.1371/journal.pone.0245481.].

[51] *Zhong DX, Zhang Y, Jin Q et al.* **Increased serum PCSK9 in patients with idiopathic pulmonary arterial hypertension: insights from inflammatory cytokines**. Pulmonary circulation 2021; 11:20458940211051292.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34659741
ABSTRACT
Proprotein convertase subtilisin/kexin type 9 (PCSK9) is an important and major player in the pathophysiology of hypercholesterolemia and atherosclerosis. Recently, PCSK9 has been implicated in the pathogenesis of inflammatory diseases. Whether PCSK9 is involved in idiopathic pulmonary arterial hypertension (IPAH) remains unclear. This study aimed to investigate the relationship between PCSK9 and IPAH. Serum PCSK9, interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), interleukin-1 β (IL-1β), and monocyte chemotactic protein-1 (MCP-1) were measured by enzyme linked immunosorbent assay. Transthoracic echocardiography was performed among 40 IPAH patients and 20 control subjects. Hemodynamic data were collected via right heart catheterization in patients with IPAH. Serum PCSK9, TNF-α, IL-6, IL-1β, and MCP-1 levels were significantly higher in IPAH patients than in control subjects ($p<0.001$). Among enrolled IPAH patients, PCSK9 levels were higher in WHO-FC III/IV patients compared with those in WHO-FC I/II ($p<0.05$), and were positively correlated with TNF-α, IL-6, MCP-1, N-Terminal pro-brain natriuretic peptide, pulmonary arterial systolic pressure ($r=0.653$, $p<0.001$), pulmonary arterial diastolic pressure ($r=0.466$, $p=0.002$), mean pulmonary arterial pressure (mPAP, $r=0.730$, <0.001), pulmonary vascular resistance ($r=0.488$, $p=0.001$), and right ventricle diameter ($r=0.563$, $p<0.001$). In multiple regression analysis, mPAP was strongly associated with serum PCSK9 ($\beta=0.694$, $p<0.001$), independent of other variables. Receiver operating characteristic curve analysis showed the optimal cutoff value of serum PCSK9 concentration for predicting IPAH was 90.67 ng/ml, with a sensitivity of 90.0% and a specificity of 85.0%. In conclusion, IPAH patients had elevated serum PCSK9 levels which correlated the presence and severity of pulmonary hypertension. PCSK9 may be a novel potential therapeutic target.

[52] *Portela-Romero M, Cinza-Sanjurjo S, Conde-Sabarís P et al.* **Real-life effect on the control of risk factors associated with initiation of the cardiovascular polypill created from equipotent drugs**. Rev Clin Esp (Barc) 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34674985

ABSTRACT

OBJECTIVE: This work aims to analyze the impact of Spain's National Center for Cardiovascular Research (CNIC-Ferrer)'s cardiovascular (CV)-polypill on blood pressure (BP) and low-density lipoprotein cholesterol (cLDL) levels in patients in our healthcare area who previously took equipotent doses of statins and antihypertensives. MATERIAL AND METHODS: All patients in our healthcare area (Santiago de Compostela, Spain) who, as of December 31, 2019, had an active prescription for the CV-polypill (CNIC-Ferrer) since January 16, 2015 were registered. The index date was the start date of the CV-polypill prescription. The drugs the patient had previously received for dyslipidemia and hypertension were analyzed, classifying them by their equivalent potency to atorvastatin and ramipril. Changes in cLDL and BP were analyzed by means of Student's t-test for paired samples. RESULTS: We analyzed 547 patients with a mean age of 71.5 ± 11.5 years. The majority were men (60.6%). We observed a decrease in cLDL (-10.6 [95% CI: -7.0, -14.3], $p < 0.001$) in patients who started taking the CV-polypill who had previously taken equally potent doses of atorvastatin (n = 471). We documented a reduction in systolic BP (-3.7 [95% CI: -0.4, -6.9], $p = 0.029$) in patients who had previously taken equally potent doses of ramipril (n = 360). In 88 patients, the CV-polypill was started via equally potent doses of atorvastatin and ramipril, with a decrease in cLDL (-8.7 [95% CI: -3.8, -13.6], $p = 0.001$) and systolic BP (-3.6 [95% CI: -7.8, 0.5], $p = 0.085$). CONCLUSIONS: The initiation of treatment with the CV-polypill in patients who previously received equally potent treatment with atorvastatin and ramipril was associated with a greater reduction in cLDL and systolic BP.

[53] *Caselli C, De Caterina R, Smit JM et al.* **Triglycerides and low HDL cholesterol predict coronary heart disease risk in patients with stable angina**. Scientific reports 2021; 11:20714.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34671067

ABSTRACT

We assessed whether high triglycerides (TG) and low high-density lipoprotein cholesterol (HDL-C) levels, expressed by an increased TG/HDL-C ratio, predict coronary atherosclerotic disease (CAD) outcomes in patients with stable angina. We studied 355 patients (60 ± 9 years, 211 males) with stable angina who underwent coronary computed tomography angiography (CTA), were managed clinically and followed for 4.5 ± 0.9 years. The primary composite outcome was all-cause mortality and non-fatal myocardial infarction. At baseline, the proportion of males, patients with metabolic syndrome, diabetes and obstructive CAD increased across TG/HDL-C ratio quartiles, together with markers of insulin resistance, hepatic and adipose tissue dysfunction and myocardial damage, with no difference in total cholesterol or LDL-C. At follow-up, the global CTA risk score (HR 1.06, 95% confidence interval (CI) 1.03-1.09, P = 0.001) and the IV quartile of the TG/HDL-C ratio (HR 2.85, 95% CI 1.30-6.26, P < 0.01) were the only independent predictors of the primary outcome. The TG/HDL-C ratio and the CTA risk score progressed over time despite increased use of lipid-lowering drugs and reduction in LDL-C. In patients with stable angina, high TG and low HDL-C levels are associated with CAD related outcomes independently of LDL-C and treatments.Trial registration. EVINCI study: ClinicalTrials.gov NCT00979199, registered September 17, 2009; SMARTool study: ClinicalTrials.gov NCT04448691, registered June 26, 2020.

[54] *Sabljić Z, Bašić-Jukić N*. **Toxic myopathy and liver damage caused by concomitant therapy with remdesivir, atorvastatin, ezetimibe, and tacrolimus in a renal transplant patient with recently treated SARS-CoV-2 induced pneumonia: A case report**. Therapeutic apheresis and dialysis : official peer-reviewed journal of the International Society for Apheresis, the Japanese Society for Apheresis, the Japanese Society for Dialysis Therapy 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34676979
ABSTRACT

[55] *Dal Pino B, Sbrana F, Bigazzi F, Sampietro T*. **Is treating severe He FH so easy? A combined treatment between lipoprotein apheresis and PCSK9 inhibitors**. Transfusion and apheresis science : official journal of the World Apheresis Association : official journal of the European Society for Haemapheresis 2021:103258.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34674949
ABSTRACT
Despite advance in pharmacotherapy of lipid disorders, many heterozygous Familial Hypercholesterolemia patients do not achieve a desirable lipid target to significantly reduce the risk of atherosclerotic cardiovascular disease. The aim of the present work is to evaluate the interaction between Lipoprotein apheresis (LA) and PCSK9i in a small FH cohort in which the guidelines therapeutic target is not achieved. During one year, together with a complete adherence to PCSK9i therapy, we recorded a 3 to 5 LA sessions less per year in each patient. This therapeutic approach suggests: i) the possibility of increasing the number of patients treated with LA, ii) the improvement of their quality of life, and iii) the costs reduction for the single patient-treatment.

[56] *Huang YQ, Li J, Chen JY, Feng YQ*. **[Prevalence trends and related factors of hypertension patients complicating with dyslipidemia in community of Guandong province between 2013 and 2018]**. Zhonghua xin xue guan bing za zhi 2021; 49:986-992.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34674436
ABSTRACT
Objective: To analyze the prevalence trends and related factors of hypertension patients complicating with dyslipidemia in community. Methods: This was a cross-sectional survey, patients with hypertension were selected from the different communities of Guangdong province in 2013 and 2018 respectively. General clinical characteristics, including demographic information, past history, family history, and medication history, were collected. Dyslipidemia was defined as follows: at least 1 item elevation of total cholesterol (TC)≥5.2 mmol/L, triglyceride (TG) ≥1.7 mmol/L, low-density lipoprotein cholesterol (LDL-C)≥3.4 mmol/L, or reduced high-density lipoprotein cholesterol (HDL-C)<1.0 mmol/L. The incidence of dyslipidemia was standardized based on the 2010 China Census data, and further subgroup analysis was performed according to age (<50, 50-60, ≥60 years old) and sex (male, female). Multivariate logistic regression was used to analyze the related factors of dyslipidemia. Results: In 2013 and 2018, 7 866 (4 148 (52.7%) females, with the age of (62.4±13.6) years) and 11 611 (6 692 (57.6%) females, with the age of (58.2±9.3)years) patients with hypertension were enrolled for data analysis, respectively. In 2013, the total prevalence rate of dyslipidemia in patients with hypertension in the community of Guangdong province was 56.3%, among which the prevalence rates of hypercholesterolemia, hypertriglyceridemia, high LDL-Cemia, and low HDL-Cemia were 17.1.

%, 21.3%, 2.3% and 24.4%, respectively. The total prevalence of dyslipidemia in patients with hypertension in the community of Guangdong in 2018 was 47.3%, prevalence of hypercholesterolemia, hypertriglyceridemia, high LDL-Cemia and low HDL-Cemia was 14.1%, 20.3%, 12.0% and 19.4%, respectively. Subgroup analysis showed that the total prevalence of dyslipidemia in male patients with hypertension in the community of Guangdong in 2013 and 2018 was 59.0% and 50.7%, respectively, among which hypercholesterolemia was 13.8% and 8.0%, and hypertriglyceridemia was 22.3%, 20.9%, high LDL-Cemia was 1.7%, 8.1%, low HDL-Cemia was 32.9%, 30.3%, respectively. In 2013 and 2018, the total prevalence of dyslipidemia in female patients with hypertension in the community of Guangdong province was 53.9% and 44.8%, among which prevalence of hypercholesterolemia was 20.5% and 18.5%, hypertriglyceridemia was 20.4% and 19.8%, and high LDL-Cemia was 2.7% and 14.9%, and hypo-HDL-Cemia was 16.8% and 11.3%, respectively. Age subgroup analysis showed that the prevalence of dyslipidemia among hypertensive patients aged<50, 50-60, and ≥60 years in Guangdong community in 2013 were 60.1%, 60.6%, and 53.7%, respectively; and 46.2%, 49.3% and 46.5% in 2018, respectively. Multivariate logistic regression analysis showed that women (OR=0.860,95%CI 0.761-0.973,P=0.017), obese (OR=2.295,95%CI 2.007-2.624,P<0.001), diabetes (OR=1.314,95%CI 1.090-1.583,P=0.004), stroke (OR=1.894,95%CI 1.227-2.924,P=0.004) and the level of fasting blood glucose (OR=1.105,95%CI 1.066-1.146,P<0.001) were independently related with the occurrence of dyslipidemia. Conclusions: The prevalence of dyslipidemia in patients with hypertension in the communities of Guangdong province is relatively high, and the prevalence differs in sex and age. Between 2013 and 2018, the total prevalence of dyslipidemia, hyper-TCemia, and hypo-HDL-Cemia in hypertensive patients shows a downward trend. The prevalence of hyper-TGemia remains unchanged, but the prevalence of high LDL-C shows an upward trend. Several factors are related to the prevalence of dislipidemia in hypertension patients in Guandong community.