[1] *Qasim S, Alamgeer, Kalsoom S et al.* **Rosuvastatin Attenuates Rheumatoid Arthritis-Associated Manifestations via Modulation of the Pro- and Anti-inflammatory Cytokine Network: A Combination of In Vitro and In Vivo Studies**. ACS Omega 2021; 6:2074-2084.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33521447

ABSTRACT

The current investigation employed rosuvastatin for evaluation as an antiarthritic agent by in vitro and in vivo studies. In vitro studies comprised egg albumin and bovine serum albumin protein denaturation assays along with membrane stabilization assays, while in vivo studies comprised formaldehyde and complete Freund's adjuvant (CFA)-provoked arthritis. The antioxidant potential was estimated via DPPH free radical scavenging and ferric reducing assays. Rosuvastatin significantly inhibited heat-provoked protein denaturation of egg albumin and bovine serum in a concentration-dependent way with the highest inhibition of 1225 ± 9.83 and 82.80 ± 4.03 at 6400 μg/mL. The percentage protection of the RBC membrane from hypotonicity-prompted lysis was found to be 80.67 ± 2.7. Rosuvastatin promisingly subdued formaldehyde-provoked arthritis, with maximum reduction (65.47%) of the paw volume being observed at a dose of 40 mg/kg. Rosuvastatin also significantly ($p < 0.001$) attenuated arthritis induced by CFA injection by reducing the paw volume and arthritic index. The reduction in the body weight due to CFA injection was also preserved by rosuvastatin treatment. Hematological and biochemical changes due to arthritis induction by CFA injection were also maintained near normal values by rosuvastatin. The histopathological and radiographic investigation also revealed the protective effect of rosuvastatin on preventing structural changes. Gene expression of IL-1β, TNF-α, and IL-6 was reduced, while IL-4 and IL-10 levels were elevated by rosuvastatin in comparison to those for the disease control group. Concentration-dependent antioxidant potential was shown by rosuvastatin. Thus, rosuvastatin possesses a notable antiarthritic potential as evidenced via in vitro and in vivo studies.

[2] *Wojda A, Janczy A, Małgorzewicz S*. **Mediterranean, vegetarian and vegan diets as practical outtakes of EAS and ACC/AHA recommendations for lowering lipid profile**. Acta biochimica Polonica 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33544561

ABSTRACT

Reduction of total cholesterol (TC) and LDL fraction (LDL-C) may be beneficial towards decreasing the risk of development of cardiovascular diseases (CVD). First and foremost, before implementing or simultaneously with pharmacological treatment, patients should be informed about lifestyle changes that may be critical to achieving a better lipid profile. Recommendations from ACC/AHA (American College of Cardiology and American Heart Association) and EAS (European Atherosclerosis Society) mainly focus on limitation of saturated fatty acids (SFA) and trans fatty acids (TFA) consumption, but additional support could be considered. This review presents selected guidelines of European scientific societies concerning lipid metabolism disorders. The main aim of this manuscript was to present the guidelines how to provide simple and transparent schemes of management in dyslipidemia therapy. Encouraging patients for increasing the intake of soluble fiber (SF) and phytosterols (PS) may also be promoted for achieving therapeutic goals. In the clinical point of view, restoring an appropriate lipid profile is important because it directly reduces the risk of developing atherosclerotic cardiovascular disease (ASCVD). The EAS and ACC/AHA guidelines introduce several new demands, so far absent from previous recommendations. Mediterranean diet

(MD) or vegetarian lifestyles are an example of diet patterns that are deliberated as healthy for cardio-vascular system, since both consist of fresh, unprocessed vegetables and fruits with addition of desirable fats.

[3] *Kananen F, Strandberg T, Loukovaara S, Immonen I*. **Early middle age cholesterol levels and the association with age-related macular degeneration**. Acta ophthalmologica 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33533136

ABSTRACT

PURPOSE: To examine whether serum cholesterol in early middle age is associated with age-related macular degeneration (AMD) later in life. METHODS: A group of Helsinki Businessmen Study (HBS) participants (n = 209) were recruited for the study. Total cholesterol (TC), triglyceride and body mass index (BMI) were measured at the HBS baseline visit in 1964-1973. Lipid subfractions, BMI, smoking status and statin use were recorded in 2011 and fundus photographs graded for AMD in 2005-2012. The subjects were genotyped for the main AMD risk single nucleotide polymorphisms (SNPs). RESULTS: TC measured at baseline 1964-1973 was significantly higher in subjects later developing intermediate or late AMD (6.67 mmol/l versus 6.20 mmol/l, p = 0.024) or with drusen size of ≥125 μm (6.68 mmol/l versus 6.21 mmol/l, p = 0.030) compared with the rest of the study population. TC, LDL and TG values at follow-up 2011 were lower in subjects with AMD compared to those without, whereas HDL levels showed no difference. In multivariate analysis, baseline TC associated with intermediate or late AMD (OR 1.59, p = 0.004) and drusen size ≥ 125 μm (OR 1.57, p = 0.006) when corrected for age, BMI, AMD risk SNPs and smoking. Lipid values measured 2011 had no associations after correction. CONCLUSIONS: High systemic total cholesterol in early middle age may have a role in the initial development of AMD, especially in patients later developing large drusen.

[4] *Khoroshinina LP, Fedorets VN, Galenko AS et al.* **[Non-traditional view on traditional risk factors of cardiovascular diseases in seniors.]**. Advances in gerontology = Uspekhi gerontologii / Rossiiskaia akademiia nauk, Gerontologicheskoe obshchestvo 2020; 33:854-860.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33550739

ABSTRACT

The article reveals little-known scientific data on the traditional risk factors of cardiovascular diseases in relation to social groups of the elderly, old people and centenarians. Some of metabolism associated signs of ageing are considering. In the article some biochemical markers in seniors are evaluated (lipids, fibrinogen, uric acid etc.). Some particularities about atherosclerotic lesions of coronary arteries in seniors are discovering, as well as relationships between coronary heart disease (CHD) and fatty liver degeneration. One more topic of the article is the lipid spectrum characteristics in senior patients with different types of heart diseases and psychological features and behavioral personality types of the seniors with cardiovascular pathology. Special attention payed on so-called preventive paradox in men older than 60 years with different forms of CHD, when the influence of traditional risk factors is critically decreased, and as important prognostic factors low levels of high-density lipoprotein cholesterol, reduced APO-A1, an increasing of APO-B/APO-A1 ratio and low physical activity play a significant role.

[5] *Baganha F, de Jong RCM, Peters EA et al.* **Atorvastatin pleiotropically decreases intraplaque angiogenesis and intraplaque haemorrhage by inhibiting ANGPT2 release and VE-Cadherin internalization**. Angiogenesis 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33550461
ABSTRACT
OBJECTIVE: Statins pleiotropically provide additional benefits in reducing atherosclerosis, but their effects on intraplaque angiogenesis (IPA) and hemorrhage (IPH) remain unclear. Therefore, we discriminated statin's lipid-lowering dependent and independent effects on IPA and IPH. APPROACH AND RESULTS: ApoE3*Leiden mice are statin-responsive due to ApoE and LDLR presence, but also allow to titrate plasma cholesterol levels by diet. Therefore, ApoE3*Leiden mice were fed a high-cholesterol-inducing-diet (HCD) with or without atorvastatin (A) or a moderate-cholesterol-inducing-diet (MCD). Mice underwent vein graft surgery to induce lesions with IPA and IPH. Cholesterol levels were significantly reduced in MCD (56%) and HCD + A (39%) compared to HCD with no significant differences between MCD and HCD + A. Both MCD and HCD + A have a similar reduction in vessel remodeling and inflammation comparing to HCD. IPA was significantly decreased by 30% in HCD + A compared to HCD or MCD. Atorvastatin treatment reduced the presence of immature vessels by 34% vs. HCD and by 25% vs. MCD, resulting in a significant reduction of IPH. Atorvastatin's anti-angiogenic capacity was further illustrated by a dose-dependent reduction of ECs proliferation and migration. Cultured mouse aortic-segments lost sprouting capacity upon atorvastatin treatment and became 30% richer in VE-Cadherin expression and pericyte coverage. Moreover, Atorvastatin inhibited ANGPT2 release and decreased VE-Cadherin(Y685)-phosphorylation in ECs. CONCLUSIONS: Atorvastatin has beneficial effects on vessel remodeling due to its lipid-lowering capacity. Atorvastatin has strong pleiotropic effects on IPA by decreasing the number of neovessels and on IPH by increasing vessel maturation. Atorvastatin improves vessel maturation by inhibiting ANGPT2 release and phospho(Y658)-mediated VE-Cadherin internalization.

[6] *Medina-Vera I, Gómez-de-Regil L, Gutiérrez-Solis AL et al.* **Dietary Strategies by Foods with Antioxidant Effect on Nutritional Management of Dyslipidemias: A Systematic Review**. Antioxidants (Basel, Switzerland) 2021; 10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33546158
ABSTRACT
Nutrition plays a fundamental role in the prevention and treatment of dyslipidemias and its oxidative-related complications. Currently, there is evidence about the beneficial effects of isolated antioxidants or foods enriched or added with antioxidant compounds. However, the application of the natural foods is more integrated than the analysis of a single nutrient. Our aim is compiling scientific literature regarding the nutritional strategies by foods with antioxidant effect in blood lipids, enzymatic and non-enzymatic antioxidants, and oxidative and inflammatory markers of subjects with dyslipidemia. We searched in MEDLINE/PubMed, Scopus, and Web of Science. From a total of 263 studies screened, 16 were included. Dietary strategies included walnuts, olive oil, raw almonds, G. paraguayase, white sesame, mate tea, Brazil nut flour, red wine, granulated Brazil nuts, grapes, wolfberry fruit, fermented beverage, coffee, orange, and blackberry juices showed significant differences in blood lipids, antioxidant activity, antioxidant enzymes, and oxidative and inflammatory markers. This systematic review compiling scientific studies about dietary strategies using foods with antioxidant effect to improve the antioxidant status in dyslipidemias.

[7] *Farnier M, Zeller M, Masson D, Cottin Y*. **Triglycerides and risk of atherosclerotic cardiovascular disease: An update**. Archives of cardiovascular diseases 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33546998

ABSTRACT

Low-density lipoprotein cholesterol is a well-known causal factor for atherosclerotic cardiovascular disease, and is the primary target of lipid-lowering therapy. There is, however, still a substantial risk of atherosclerotic cardiovascular disease events despite intensive statin therapy, and data from clinical trials suggest that an elevated concentration of triglycerides is a marker of residual cardiovascular risk on low-density lipoprotein-lowering therapy. Serum triglycerides are a biomarker for triglyceride-rich lipoproteins, and several lines of evidence indicate that triglyceride-rich lipoproteins and their cholesterol-enriched remnant particles are associated with atherogenesis. Moreover, genetic data in humans strongly suggest that the remnants of triglyceride-rich lipoproteins are a causal cardiovascular risk factor. Although lifestyle changes remain the cornerstone of management of hypertriglyceridaemia, a recent trial with high doses of the omega-3 fatty acid icosapent ethyl showed a significant reduction in cardiovascular events that was not explained by the reduction in triglycerides alone. In patients with elevated triglycerides, several novel drugs are in development to reduce the residual risk on statin therapy linked to an excess of atherogenic triglyceride-rich lipoproteins. In this review, we provide an update on the biology, epidemiology and genetics of triglycerides, and the risk of atherosclerotic cardiovascular disease.

[8] *Hu D, Guo Y, Wu R et al.* **New Insight Into Metformin-Induced Cholesterol-Lowering Effect Crosstalk Between Glucose and Cholesterol Homeostasis via ChREBP (Carbohydrate-Responsive Element-Binding Protein)-Mediated PCSK9 (Proprotein Convertase Subtilisin/Kexin Type 9) Regulation**. Arteriosclerosis, thrombosis, and vascular biology 2021:Atvbaha120315708.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33535788

ABSTRACT

OBJECTIVE: Metformin, a first-line drug for treating individuals with type 2 diabetes, exerts beneficial effects on cholesterol-lowering, yet its precise mechanism has not been established. Approach and Results: In 2 dyslipidemia mouse models, administration of metformin significantly decreased serum cholesterol and PCSK9 (proprotein convertase subtilisin/kexin type 9) levels, accompanied by decreased expression of PCSK9 in both mRNA and protein levels resulting in a 3-fold increase of LDLR (low-density lipoprotein receptor) in the liver. In human hepatocytes, metformin treatment suppressed the PCSK9 transcription. Depressed transcription was driven by a glucose sensor, the ChREBP (carbohydrate-responsive element-binding protein) but not by the intracellular cholesterol sensor, the SREBP2 (sterol regulatory element-binding protein 2). We further identified PCSK9 as a novel target gene of ChREBP. Metformin decreased the expression of ChREBP and inhibited its transcriptional activity by blocking its nuclear translocation attributed to the decreased intracellular glucose and glucose metabolites levels. Moreover, metformin treatment significantly decreased serum low-density lipoprotein cholesterol and PCSK9 levels in nondiabetic individuals. CONCLUSIONS: Collectively, we revealed a new mechanism of action of metformin in cholesterol-lowering and identified a novel crosstalk signal between glucose and cholesterol homeostasis via ChREBP-mediated PCSK9 regulation.

[9] *Lee HY, Ahn J, Park J et al.* **Beneficial Effect of Statins in COVID-19-Related Outcomes: A National Population-Based Cohort Study**. Arteriosclerosis, thrombosis, and vascular biology 2021:Atvbaha120315551.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33535790

ABSTRACT

OBJECTIVE: Although statins are widely prescribed lipid-lowering drugs, there are concerns about the safety of their use in the context of coronavirus disease 2019 (COVID-19), since statins increase the expression of ACE2. This study aimed to disclose the association between statins and 60-day COVID-19 mortality. Approach and Results: All patients hospitalized with laboratory-confirmed COVID-19 were enrolled in this study from January 19 to April 16, 2020, in Korea. We evaluated the association between the use of statins and COVID-19-related mortality in the overall and the nested 1:2 propensity score-matched study. Furthermore, a comparison of the hazard ratio for death was performed between COVID-19 patients and a retrospective cohort of patients hospitalized with pneumonia between January and June 2019 in Korea. The median age of the 10 448 COVID-19 patients was 45 years. Statins were prescribed in 533 (5.1%) patients. After adjusting for age, sex, and comorbidities, Cox regression showed a significant decrease in hazard ratio associated with the use of statins (hazard ratio, 0.637 [95% CI, 0.425-0.953]; P=0.0283). Moreover, on comparing the hazard ratio between COVID-19 patients and the retrospective cohort of hospitalized pneumonia patients, the use of statins showed similar benefits. CONCLUSIONS: The use of statins correlates significantly with lower mortality in patients with COVID-19, consistent with the findings in patients with pneumonia.

[10] *Marco-Benedí V, Laclaustra M, Bea AM et al.* **Maternally inherited hypercholesterolemia does not modify the cardiovascular phenotype in familial hypercholesterolemia**. Atherosclerosis 2021; 320:47-52.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33529866

ABSTRACT

BACKGROUND AND AIMS: Familial hypercholesterolemia (FH) is a codominant autosomal disease characterized by a high risk of cardiovascular disease when not in lipid-lowering treatment. However, there is a large variability in the clinical presentation in heterozygous subjects (HeFH). Maternal hypercholesterolemia has been proposed as a cardiometabolic risk factor later in life. Whether this phenotype variability depends on the mother or father origin of hypercholesterolemia is unknown. The objective of this study was to analyze potential differences in anthropometry, superficial lipid deposits, comorbidities, and lipid concentrations depending on the parental origin of hypercholesterolemia within a large group of HeFH. METHODS: This is a cross-sectional observational, multicenter, nation-wide study in Spain. We recruited adults with HeFH to study clinical differences according to the parental origin. Data on HeFH patients were obtained from the Dyslipidemia Registry of the Spanish Atherosclerosis Society. RESULTS: HeFH patients were grouped in 1231 HeFH-mother-offspring aged 45.7 (16.3) years and 1174 HeFH-father-offspring aged 44.8 (16.7) years. We did not find any difference in lipid parameters (total cholesterol, triglycerides, LDLc, HDLc, and Lp(a)), nor in the comorbidities studied (cardiovascular disease prevalence, age of onset of cardiovascular disease, obesity, diabetes, and hypertension) between groups. Lipid-lowering treatment did not differ between groups. The prevalence of comorbidities did not show differences when they were studied by age

groups. CONCLUSIONS: Our research with a large group of subjects with HeFH shows that a potential maternal effect is not relevant in FH. However, due to the size of our sample, potential differences between genders cannot be completely ruled out. This implies that severe maternal hypercholesterolemia during pregnancy is not associated with additional risk in the FH affected offspring.

[11] *Vuorio A, Raal F, Kaste M, Kovanen PT*. **Familial hypercholesterolaemia and COVID-19: A two-hit scenario for endothelial dysfunction amenable to treatment**. Atherosclerosis 2021; 320:53-60.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33540179
ABSTRACT
Patients with familial hypercholesterolemia (FH) are likely at increased risk for COVID-19 complications in the acute phase of the infection, and for a long time thereafter. Because in FH patients the level of low density lipoprotein cholesterol (LDL-C) is elevated from birth and it correlates with the degree of systemic endothelial dysfunction, both heterozygous FH (HeFH) patients and, in particular, homozygous FH (HoFH) patients have a dysfunctional endothelium prone to further damage by the direct viral attack and the hyper-inflammatory reaction typical of severe COVID-19. Evidence to date shows the benefit of statin use in patients with COVID-19. In FH patients, the focus should therefore be on the effective lowering of LDL-C levels, the root cause of the expected excess vulnerability to COVID-19 infection in these patients. Moreover, the ongoing use of statins and other lipid-lowering therapies should be encouraged during the COVID pandemic to mitigate the risk of cardiovascular complications from COVID-19. For the reduction of the excess risk in FH patients with COVID-19, we advocate stringent adherence to the guideline determined LDL-C levels for FH patients, or maybe even to lower levels. Unfortunately, epidemiologic data are lacking on the severity of COVID-19 infections, as well as the number of acute cardiac events that have occurred in FH subjects during the COVID-19 pandemic. Such data need to be urgently gathered to learn how much the risk for, and the severity of COVID-19 in FH are increased.

[12] *Namdarimoghaddam P, Fowokan A, Humphries KH et al.* **Association of "hypertriglyceridemic waist" with increased 5-year risk of subclinical atherosclerosis in a multi-ethnic population: a prospective cohort study**. BMC cardiovascular disorders 2021; 21:63.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33530949
ABSTRACT
BACKGROUND: Hypertriglyceridemic waist (HTGW), which incorporates measures of waist circumference and levels of triglyceride in blood, could act as an early-stage predictor to identify the individuals at high-risk for subclinical atherosclerosis. Previous studies have explored the cross-sectional association between HTGW and atherosclerosis; however, understanding how this association might change over time is necessary. This study will assess the association between HTGW with 5-year subclinical carotid atherosclerosis. METHODS: 517 participants of Aboriginal, Chinese, European, and South Asian ethnicities were examined for baseline HTGW and 5-year indices of subclinical atherosclerosis (intima media thickness (mm), total area (mm(2)), and plaque presence). Family history of cardiovascular disease, sociodemographic measures (age, sex, ethnicity, income level, maximum education), and traditional risk factors (systolic blood pressure, smoking status, total cholesterol, high-density lipoprotein cholesterol, body mass index) were incorporated into

the models of association. These models used multiple linear regression and logistic regression. RESULTS: Baseline HTGW phenotype is a statistically significant and clinically meaningful predictor of 5-year intima media thickness (β = 0.08 [0.04, 0.11], p < 0.001), total area (β = 0.20 [0.07, 0.33], p = 0.002), and plaque presence (OR = 2.17 [1.13, 4.19], p = 0.02) compared to the non-HTGW group independent of sociodemographic factors and family history. However, this association is no longer significant after adjusting for the traditional risk factors of atherosclerosis (p = 0.27, p = 0.45, p = 0.66, respectively). Moreover, change in status of HTGW phenotype does not correlate with change in indices of atherosclerosis over 5 years. CONCLUSIONS: Our results suggest that when the traditional risk factors of atherosclerosis are known, HTGW may not offer additional value as a predictor of subclinical atherosclerosis progression over 5 years.

[13] *Zhao X, Wang D, Qin L*. **Lipid profile and prognosis in patients with coronary heart disease: a meta-analysis of prospective cohort studies**. BMC cardiovascular disorders 2021; 21:69.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33535982
ABSTRACT
BACKGROUND: This meta-analysis based on prospective cohort studies aimed to evaluate the associations of lipid profiles with the risk of major adverse cardiovascular outcomes in patients with coronary heart disease (CHD). METHODS: The PubMed, Embase, and Cochrane Library electronic databases were systematically searched for prospective cohort study published through December 2019, and the pooled results were calculated using the random-effects model. RESULTS: Twenty-one studies with a total of 76,221 patients with CHD met the inclusion criteria. The per standard deviation (SD) increase in triglyceride was associated with a reduced risk of major adverse cardiovascular events (MACE). Furthermore, the per SD increase in high-density lipoprotein cholesterol (HDL-C) was associated with a reduced risk of cardiac death, whereas patients with lower HDL-C were associated with an increased risk of MACE, all-cause mortality, and cardiac death. Finally, the risk of MACE was significantly increased in patients with CHD with high lipoprotein(a) levels. CONCLUSIONS: The results of this study suggested that lipid profile variables could predict major cardiovascular outcomes and all-cause mortality in patients with CHD.

[14] *Drechsler H, Ayers C, Cutrell J et al.* **Consistent use of lipid lowering therapy in HIV infection is associated with low mortality**. BMC infectious diseases 2021; 21:150.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33546621
ABSTRACT
BACKGROUND: In people living with HIV (PLWH), statins may be disproportionately effective but remain underutilized. A large prospective trial in patients with low to moderate cardiovascular (ASCVD) risk will reveal whether they should be considered in all PLWH. But its effect size may not apply to real-world PLWH with higher ASCVD and mortality risk. Also, the clinical role of non-statin lipid-lowering therapy (LLT) and LLT adherence in this population is unknown. METHODS: Comparative multi-level marginal structural model for all-cause mortality examining four time-updated exposure levels to LLT, antihypertensives, and aspirin in a virtual cohort of older PLWH. Incident coronary, cerebrovascular, and overall ASCVD events, serious infections, and new cancer diagnoses served as explanatory outcomes. RESULTS: In 23,276 HIV-infected US-veterans who were followed for a median of 5.2 years after virologic suppression overall mortality was 33/1000 patient years: >3 times higher than in the US population. Use of antihypertensives or aspirin was associated with

increased mortality. Past LLT use (>1 year ago) had no effect on mortality. LLT exposure in the past year was associated with a reduced hazard ratio (HR) of death: 0.59, 95% confidence interval (CI) 0.51-0.69, p<0.0001 for statin containing LLT and 0.71 (CI: 0.54-0.93), p=0.03 for statin-free LLT. For consistent LLT use (>11/12 past months) the HR of death was 0.48 (CI: 0.35-0.66) for statin-only LLT, 0.34 (CI: 0.23-0.52) for combination LLT, and 0.27 (CI: 0.15-0.48) for statin-free LLT (p<0.0001 for all). The ASCVD risk in these patients was reduced in similar fashion. Use of statin containing LLT was also associated with reduced infection and cancer risk. Multiple contrasting subgroup analyses yielded comparable results. Confounding is unlikely to be a major contributor to our findings. CONCLUSIONS: In PLWH, ongoing LLT use may lead to substantially lower mortality, but consistent long-term adherence may be required to reduce ASCVD risk. Consistent non-statin LLT may be highly effective and should be studied prospectively.

[15] *Ma TT, Wong ICK, Whittlesea C et al.* **Impact of multiple cardiovascular medications on mortality after an incidence of ischemic stroke or transient ischemic attack**. BMC medicine 2021; 19:24.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33530992
ABSTRACT
BACKGROUND: To manage the risk factors and to improve clinical outcomes, patients with stroke commonly receive multiple cardiovascular medications. However, there is a lack of evidence on the optimum combination of medication therapy in the primary care setting after ischemic stroke. Therefore, this study aimed to investigate the effect of multiple cardiovascular medications on long-term survival after an incident stroke event (ischemic stroke or transient ischemic attack (TIA)). METHODS: This study consisted of 52,619 patients aged 45 and above with an incident stroke event between 2007 and 2016 in The Health Improvement Network database. We estimated the risk of all-cause mortality in patients with multiple cardiovascular medications versus monotherapy using a marginal structural model. RESULTS: During an average follow-up of 3.6 years, there were 9230 deaths (7635 in multiple cardiovascular medication groups and 1595 in the monotherapy group). Compared with patients prescribed monotherapy only, the HRs of mortality were 0.82 (95% CI 0.75-0.89) for two medications, 0.65 (0.59-0.70) for three medications, 0.61 (0.56-0.67) for four medications, 0.60 (0.54-0.66) for five medications and 0.66 (0.59-0.74) for ≥six medications. Patients with any four classes of antiplatelet agents (APAs), lipid-regulating medications (LRMs), angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin receptor blockers (ARBs), beta-blockers, diuretics and calcium channel blockers (CCBs) had the lowest risk of mortality (HR 0.51, 95% CI 0.46-0.57) versus any one class. The combination containing APAs, LRMs, ACEIs/ARBs and CCBs was associated with a 61% (95% CI 53-68%) lower risk of mortality compared with APAs alone. CONCLUSION: Our results suggested that combination therapy of four or five cardiovascular medications may be optimal to improve long-term survival after incident ischemic stroke or TIA. APAs, LRMs, ACEIs/ARBs and CCBs were the optimal constituents of combination therapy in the present study.

[16] *Choi JY, Choi CU, Choi BG et al.* **New onset diabetes mellitus and cardiovascular events in Korean patients with acute myocardial infarction receiving high-intensity statins**. BMC pharmacology & toxicology 2021; 22:11.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33541430

ABSTRACT
BACKGROUND: High-intensity statin therapy is typically used in patients with acute myocardial infarction (AMI) for secondary prevention. However, there have been consistent concerns regarding its association with diabetes mellitus. We investigated the effect of high-intensity atorvastatin and rosuvastatin on new-onset diabetes mellitus (NODM) and cardiovascular outcomes over a 3-year follow-up period. METHODS: Data from the Korea Acute Myocardial Infarction Registry were collected from November 2011 to October 2015, and 13,104 patients with AMI were enrolled from major cardiovascular centers. Among them, 2221 patients without diabetes who had been administered with high-intensity atorvastatin (40-80 mg) and rosuvastatin (20 mg) were investigated. The atorvastatin and rosuvastatin groups were evaluated for the incidence of NODM and major adverse cardiac events (MACE) including death, myocardial infarction, and revascularization cases in the following 3 years. RESULTS: Baseline characteristics were comparable between the two groups. Event-free survival rate of NODM was not significantly different between the atorvastatin and rosuvastatin groups (92.5% vs. 90.8%, respectively; Log-rank P-value = 0.550). The event-free survival rate of MACE was also not significantly different between atorvastatin and rosuvastatin groups (89.0% vs. 89.6%, respectively; Log rank P-value = 0.662). Multivariate Cox analysis revealed that statin type was not a prognostic factor in the development of NODM and MACE. CONCLUSIONS: Administering high-intensity atorvastatin and rosuvastatin in patients with AMI produced comparable effects on NODM and clinical outcomes, suggesting their clinical equivalence in secondary prevention.

[17] *Scholl JG*. **Does a ketogenic diet lower a very high Lp(a)? A striking experiment in a male physician**. BMJ Nutr Prev Health 2020; 3:413-415.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33521554

ABSTRACT
The level of lipoprotein(a) (Lp(a)), an important cardiovascular risk factor, is considered to be genetically determined. I am a 55-year-old male physician specialised in preventive medicine and a hobby triathlete with a body mass index of 24.9 kg/m(2) and a maximum oxygen consumption (VO(2)max) of ~50 mL/(kg×min), with an average of 7-10 hours of exercise per week. I discovered my own Lp(a) at 92-97 mg/dL in 2004 and measured a maximum Lp(a) of 108 mg/dL in 2013. Surprisingly, I observed a much lower Lp(a) of 65 mg/dL in 2018. This happened after I had adopted a very-low-carb ketogenic diet for long-term endurance exercise. My n=1 experiment in July 2020 demonstrated an increase in Lp(a) back to 101 mg/dL on a very high-carb diet within 2 weeks, and a drop back to 74 mg/dL after 3 weeks on the ketogenic diet afterwards. The observed large changes in my Lp(a) were thus reproducible by a change in carbohydrate consumption and might have clinical relevance for patients as well as researchers in the field of Lp(a).

[18] *Hadaegh F, Asgari S, Toreyhi H et al.* **Sex-Specific Incidence Rates and Risk Factors for Fracture: A 16-year Follow-up from The Tehran Lipid and Glucose Study**. Bone 2021:115869.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33529827

ABSTRACT
OBJECTIVE: To examine the population-based incidence of any-fracture and its potential risk factors in a sex-split cohort of the Iranian population. MATERIALS AND METHODS: A total of 3,477 men and 4,085 women with a mean (SD) age of 47.92(13.1) and 45.88(11.47) years, respectively were

entered into the study. The age-standardized incidence rates per 100,000 person-years were reported for the whole population and each sex separately. Cox proportional hazard models were used to estimate hazard ratios (HR) for potential risk factors. Only fractures requiring inpatients' care were considered as the outcome. We also defined major osteoporotic fractures (MOF) as the composite of the fractures that occurred in the vertebral, wrist, hip and pelvic sites among population aged ≥50 years. RESULTS: During the median (IQR) follow-up of 15.9 years, 4.34%men and 3.75% women experienced at least one incident any-fracture. The annual age-standardized incidence rates (95% CI) among men and women were 330.9 (279.6-388.9) and 319.4(268.1-377.3) per 100,000 person-years, respectively; the corresponding values for incidence of MOF was 202.2(142.3-278.6) in men and 342.01(260.4-441.0) per 100,000 person-years for women. In the multivariable model, among the whole population, age groups ≥50 years, central obesity [HR: 95% CI 1.77(1.32-2.39)], current smoking [1.59(1.15-2.20)] and using steroid medications [2.20(1.04-4.67)] significantly increased the risk of incident fracture (all P <0.05); however the impact of the first two risk factors were more prominent among women (P for interaction ≤ 0.01). Moreover, being obese was associated with a lower risk of incident first fracture in the total population [HR: 95% CI: 0.61(0.40-0.92)]. Being men [HR: 95% CI: 0.54(0.30-0.99)] and prediabetes status [HR: 95% CI: 0.53(0.30-0.95)] were also associated with lower risk for MOF. CONCLUSION: This is the first report of long-term incidence rate of any-fracture and MOF in a conducted in the metropolitan city of Tehran. Among modifiable risk factors of fracture, in the whole population smoking habit and using steroid medications and particularly for women central obesity should be considered as main risk factors for preventive strategies. Prediabetes status was associated with lower risk of MOF.

[19] *Badreldeen A, El Razaky O, Erfan A et al.* **Comparative study of the efficacy of captopril, simvastatin, and L-carnitine as cardioprotective drugs in children with type 1 diabetes mellitus: a randomised controlled trial**. Cardiology in the young 2021:1-8.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33536102

ABSTRACT

OBJECTIVES: To assess the efficacy and safety of captopril, simvastatin, and L-carnitine as cardioprotective drugs in children with type 1 diabetes mellitus on different echocardiographic parameters, electrocardiographic parameter, lipid profile, and carotid intima-media thickness. METHODS: This randomised controlled trial was conducted on 100 children with type 1 diabetes mellitus for more than 3 years during the period from September 2018 to June 2020. Fifty healthy children of matched age and sex served as a control group. The patients were randomly assigned into four groups (25 children each): no-treatment group who received no cardioprotective drug, simvastatin group who received simvastatin (10-20 mg/day), captopril group who received captopril (0.2 mg/kg/day), and L-carnitine group who received L-carnitine (50 mg/kg/day) for 4 months. Lipid profile, serum troponin I, carotid intima-media thickness, and echocardiographic examinations were performed on all included children before and after the treatment. RESULTS: Total cholesterol and low-density lipoprotein were significantly decreased in children who received simvastatin or L-carnitine. Triglycerides significantly decreased only in children who received simvastatin. High-density lipoprotein significantly increased in simvastatin and L-carnitine groups only. Serum troponin I decreased significantly in all the three treatment groups. Carotid intima-media thickness showed no significant change in all treatment groups. Echocardiographic parameters significantly improved in simvastatin, L-carnitine, and captopril groups. CONCLUSION: Captopril, simvastatin, and L-carnitine

have a significant beneficial effect on cardiac functions in children with type 1 diabetes mellitus. However, only simvastatin and L-carnitine have a beneficial effect on the lipid profile. The drugs were safe and well tolerated.Clinical trial registration: The clinical trial was registered at www.clinicaltrial.gov (NCT03660293).

[20] *Cosson E, Nguyen MT, Rezgani I et al.* **Epicardial adipose tissue volume and coronary calcification among people living with diabetes: a cross-sectional study**. Cardiovascular diabetology 2021; 20:35.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33546697
ABSTRACT
BACKGROUND: Epicardial adipose tissue (EAT) has anatomic and functional proximity to the heart and is considered a novel diagnostic marker and therapeutic target in cardiometabolic diseases. The aim of this study was to evaluate whether EAT volume was associated with coronary artery calcification (CAC) in people living with diabetes, independently of confounding factors. METHODS: We included all consecutive patients with diabetes whose EAT volume and CAC score were measured using computed tomography between January 1, 2019 and September 30, 2020 in the Department of Diabetology-Endocrinology-Nutrition at Avicenne Hospital, France. Determinants of EAT volume and a CAC score ≥ 100 Agatston units (AU) were evaluated. RESULTS: The study population comprised 409 patients (218 men). Mean (± standard deviation) age was 57 ± 12 years, and 318, 56 and 35 had type 2 (T2D), type 1 (T1D), or another type of diabetes, respectively. Mean body mass index (BMI) was 29 ± 6 kg/m(2), mean AET volume 93 ± 38 cm(3). EAT volume was positively correlated with age, BMI, pack-year smoking history and triglyceridaemia, but negatively correlated with HDL-cholesterol level. Furthermore, it was lower in people with retinopathy, but higher in men, in Caucasian people, in patients on antihypertensive and lipid-lowering medication, in people with nephropathy, and finally in individuals with a CAC ≥ 100 AU (CAC < 100 vs CAC ≥ 100: 89 ± 35 vs 109 ± 41 cm(3), respectively, $p < 0.05$). In addition to EAT volume, other determinants of CAC ≥ 100 AU (n = 89, 22%) were age, T2D, ethnicity, antihypertensive and lipid-lowering medication, cumulative tobacco consumption, retinopathy, macular edema and macrovascular disease. Multivariable analysis considering all these determinants as well as gender and BMI showed that EAT volume was independently associated with CAC ≥ 100 AU (per 10 cm(3) increase: OR 1.11 [1.02-1.20]). CONCLUSIONS: EAT volume was independently associated with CAC. As it may play a role in coronary atherosclerosis in patients with diabetes, reducing EAT volume through physical exercise, improved diet and pharmaceutical interventions may improve future cardiovascular risk outcomes in this population.

[21] *Yu D, Liao JK*. **Emerging views of statin pleiotropy and cholesterol lowering**. Cardiovascular research 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33533892
ABSTRACT
Over the past four decades, no class of drugs has had more impact on cardiovascular health than the HMC-CoA reductase inhibitors or statins. Developed as potent lipid-lowering agents, statins were later shown to reduce morbidity and mortality of patients who are at risk for cardiovascular disease. However, retrospective analyses of some of these clinical trials have uncovered some aspects of their clinical benefits that may be additional to their lipid-lowering effects. Such "pleiotropic" effects of

statins garnered intense interest and debate over its contribution to cardiovascular risk reduction. This review will provide a brief background of statin pleiotropy, assess the available clinical evidence for and against their non-lipid-lowering benefits, and propose future research directions in this field.

[22] *Drucker DJ*. **Diabetes, obesity, metabolism, and SARS-CoV-2 infection: the end of the beginning**. Cell Metab 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33529600
ABSTRACT
The increased prevalence of obesity, diabetes, and cardiovascular risk factors in people hospitalized with severe COVID-19 illness has engendered considerable interest in the metabolic aspects of SARS-CoV-2-induced pathophysiology. Here, I update concepts informing how metabolic disorders and their co-morbidities modify the susceptibility to, natural history, and potential treatment of SARS-CoV-2 infection, with a focus on human biology. New data informing genetic predisposition, epidemiology, immune responses, disease severity, and therapy of COVID-19 in people with obesity and diabetes are highlighted. The emerging relationships of metabolic disorders to viral-induced immune responses and viral persistence, and the putative importance of adipose and islet ACE2 expression, glycemic control, cholesterol metabolism, and glucose- and lipid-lowering drugs is reviewed, with attention to controversies and unresolved questions. Rapid progress in these areas informs our growing understanding of SARS-CoV-2 infection in people with diabetes and obesity, while refining the therapeutic strategies and research priorities in this vulnerable population.

[23] *Liu T, Yoon WS, Lee SR*. **Recent Updates of Lipoprotein(a) and Cardiovascular Disease**. Chonnam medical journal 2021; 57:36-43.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33537217
ABSTRACT
In recent years, epidemiological studies, genome-wide association studies, and Mendelian randomization studies have shown a strong association between increased levels of lipoproteins and increased risks of coronary heart disease and cardiovascular disease (CVD). Although lipoprotein(a) [Lp(a)] was an independent risk factor for ASCVD, the latest international clinical guidelines do not recommend direct reduction of plasma Lp(a) concentrations. The main reason was that there is no effective clinical medicine that directly lowers plasma Lp(a) concentrations. However, recent clinical trials have shown that proprotein convertase subtilisin/kexin-type 9 inhibitors (PCSK9) and second-generation antisense oligonucleotides can effectively reduce plasma Lp(a) levels. This review will present the structure, pathogenicity, prognostic evidences, and recent advances in therapeutic drugs for Lp(a).

[24] *Caro L, Prueksaritanont T, Fandozzi CM et al.* **Evaluation of Pharmacokinetic Drug Interactions of the Direct-Acting Antiviral Agents Elbasvir and Grazoprevir with Pitavastatin, Rosuvastatin, Pravastatin, and Atorvastatin in Healthy Adults**. Clinical drug investigation 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33527237
ABSTRACT
BACKGROUND: Many people infected with hepatitis C virus have comorbidities, including hypercholesterolemia, that are treated with statins. In this study, we evaluated the drug-drug interaction potential of the hepatitis C virus inhibitors elbasvir (EBR) and grazoprevir (GZR) with

statins. Pitavastatin, rosuvastatin, pravastatin, and atorvastatin are substrates of organic anion-transporting polypeptide 1B, whereas rosuvastatin and atorvastatin are also breast cancer resistance protein substrates. METHODS: Three open-label, phase I clinical trials in healthy adults were conducted with multiple daily doses of oral GZR or EBR/GZR and single oral doses of statins. Trial 1: GZR 200 mg plus pitavastatin 10 mg. Trial 2: Part 1, GZR 200 mg plus rosuvastatin 10 mg, then EBR 50 mg/GZR 200 mg plus rosuvastatin 10 mg; Part 2, EBR 50 mg/GZR 200 mg plus pravastatin 40 mg. Trial 3: EBR 50 mg/GZR 200 mg plus atorvastatin 10 mg. RESULTS: Neither GZR nor EBR pharmacokinetics were meaningfully affected by statins. Coadministration of EBR/GZR did not result in clinically relevant changes in the exposure of pitavastatin or pravastatin. However, EBR/GZR increased exposure to rosuvastatin (126%) and atorvastatin (94%). Coadministration of statins plus GZR or EBR/GZR was generally well tolerated. CONCLUSIONS: Although statins do not appreciably affect EBR or GZR pharmacokinetics, EBR/GZR can impact the pharmacokinetics of certain statins, likely via inhibition of breast cancer resistance protein but not organic anion-transporting polypeptide 1B. Coadministration of EBR/GZR with pitavastatin or pravastatin does not require adjustment of either dose of statin, whereas the dose of rosuvastatin and atorvastatin should be decreased when coadministered with EBR/GZR.

[25] *Alkhalil M*. **Novel tools for new therapies in the era of contemporary percutaneous coronary revascularisation**. Current cardiology reviews 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33530910
ABSTRACT
Percutaneous coronary intervention (PCI) is an expanding treatment option for patients with coronary artery disease (CAD). It is considered the default strategy for unstable presentation of CAD. PCI techniques have evolved over the last 4 decades with significant improvements in stent design, increase in functional assessment of coronary lesions, and the use of intra-vascular imaging. Nonetheless, the morbidity and mortality related to CAD remain significant. Advances in technology have allowed better understanding of the nature andprogression of CAD. New tools are now available that reflect the pathophysiological changes at the level of the myocardium and coronary atherosclerotic plaque. Certain changes within the plaque would render it more prone to rupture leading to acute vascular events. These changes are potentially detected using novel tools invasively, such near infra-red spectroscopy, or non-invasively using T2 mapping cardiovascular magnetic resonance imaging (CMR)and18F-Sodium Fluoride positron emission tomography/computed tomography. Similarly, changes at the level of the injured myocardium are feasibly assessed invasively using index microcirculatory resistance or non-invasively using T1 mapping CMR. Importantly, these changes could be detected immediately with the opportunity to tailor treatment to those considered at high risk. Concurrently, novel therapeutic options have demonstrated promising results in reducingfuture cardiovascular risks in patients with CAD. This Review article will discuss the role of these novel tools and their applicability in employing mechanical and pharmacological treatment to mitigate cardiovascular risk in patients with CAD.

[26] *Vergès B, Duvillard L, Pais de Barros JP et al.* **Liraglutide Increases the Catabolism of Apolipoprotein B100-Containing Lipoproteins in Patients With Type 2 Diabetes and Reduces Proprotein Convertase Subtilisin/Kexin Type 9 Expression**. Diabetes Care 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33531418

ABSTRACT
OBJECTIVE: Dyslipidemia observed in type 2 diabetes (T2D) is atherogenic. Important features of diabetic dyslipidemia are increased levels of triglyceride-rich lipoproteins and small dense LDL particles, which all have apolipoprotein B100 (apoB100) as a major apolipoprotein. This prompted us to study the effect of the GLP-1 agonist liraglutide on the metabolism of apoB100-containing lipoproteins. RESEARCH DESIGN AND METHODS: We performed an in vivo kinetic study with stable isotopes (L-[1-(13)C]leucine) in 10 patients with T2D before and after 6 months of treatment with liraglutide (1.2 mg/day). We also evaluated in mice the effect of liraglutide on the expression of genes involved in apoB100-containing lipoprotein clearance. RESULTS: In patients with T2D, liraglutide treatment significantly reduced plasma apoB100 (0.93 ± 0.13 vs. 1.09 ± 0.11 g/L, P = 0.011) and fasting triglycerides (1.76 ± 0.37 vs. 2.48 ± 0.69 mmol/L, P = 0.005). The kinetic study showed a significant increase in indirect catabolism of VLDL(1)-apoB100 (4.11 ± 1.91 vs. 2.96 ± 1.61 pools/day, P = 0.005), VLDL(2)-apoB100 (5.17 ± 2.53 vs. 2.84 ± 1.65 pools/day, P = 0.008), and IDL-apoB100 (5.27 ± 2.77 vs. 3.74 ± 1.85 pools/day, P = 0.017) and in catabolism of LDL-apoB100 (0.72 ± 0.22 vs. 0.56 ± 0.22 pools/day, P = 0.005). In mice, liraglutide increased lipoprotein lipase (LPL) gene expression and reduced proprotein convertase subtilisin/kexin type 9 (PCSK9), retinol-binding protein 4 (RBP4), and tumor necrosis factor-α (TNF-α) gene expression in adipose tissue and decreased PCSK9 mRNA and increased LDL receptor protein expression in liver. In vitro, liraglutide directly reduced the expression of PCSK9 in the liver. CONCLUSIONS: Treatment with liraglutide induces a significant acceleration of the catabolism of triglyceride-rich lipoproteins (VLDL(1), VLDL(2), IDL) and LDL. Liraglutide modifies the expression of genes involved in apoB100-containing lipoprotein catabolism. These positive effects on lipoprotein metabolism may reduce cardiovascular risk in T2D.

[27] *Virani SS, Nambi V, Ballantyne CM*. **Has the "strength" of fish oil therapy been "reduced"? reconciling the results of REDUCE-IT and STRENGTH**. European heart journal. Cardiovascular pharmacotherapy 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33537734
ABSTRACT

[28] *Limonova AS, Ershova AI, Meshkov AN et al.* **Case Report: Hypertriglyceridemia and Premature Atherosclerosis in a Patient With Apolipoprotein E Gene ε2ε1 Genotype**. Frontiers in cardiovascular medicine 2020; 7:585779.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33537346
ABSTRACT
We present a case of a 40-year-old male with premature atherosclerosis, with evidence of both eruptive and tendinous xanthomas, which could imply an increase in both low-density lipoprotein (LDL) and triglyceride (TG) levels. However, his LDL was 2.08 mmol/l, TG -11.8 mmol/l on rosuvastatin 20 mg. Genetic evaluation was performed using a custom panel consisting of 25 genes and 280 variants responsible for lipid metabolism. A rare ε2ε1 genotype of apolipoprotein E was detected. The combination of clinical manifestations and genetic factors in this patient leads to the diagnosis of familial dysbetalipoproteinemia. Implementation of genetic testing into routine clinical practice could not only improve disease diagnostics and management, but also help prevent their development.

[29] *Kamar A, Khalil A, Nemer G*. **The Digenic Causality in Familial Hypercholesterolemia: Revising the Genotype-Phenotype Correlations of the Disease**. Frontiers in genetics 2020; 11:572045.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33519890
ABSTRACT
Genetically inherited defects in lipoprotein metabolism affect more than 10 million individuals around the globe with preponderance in some parts where consanguinity played a major role in establishing founder mutations. Mutations in four genes have been so far linked to the dominant and recessive form of the disease. Those players encode major proteins implicated in cholesterol regulation, namely, the low-density lipoprotein receptor (LDLR) and its associate protein 1 (LDLRAP1), the proprotein convertase substilin/kexin type 9 (PCSK9), and the apolipoprotein B (APOB). Single mutations or compound mutations in one of these genes are enough to account for a spectrum of mild to severe phenotypes. However, recently several reports have identified digenic mutations in familial cases that do not necessarily reflect a much severe phenotype. Yet, data in the literature supporting this notion are still lacking. Herein, we review all the reported cases of digenic mutations focusing on the biological impact of gene dosage and the potential protective effects of single-nucleotide polymorphisms linked to hypolipidemia. We also highlight the difficulty of establishing phenotype-genotype correlations in digenic familial hypercholesterolemia cases due to the complexity and heterogeneity of the phenotypes and the still faulty in silico pathogenicity scoring system. We finally emphasize the importance of having a whole exome/genome sequencing approach for all familial cases of familial hyperlipidemia to better understand the genetic and clinical course of the disease.

[30] *Sikharulidze I, Chelidze K, Mamatsashvili I*. **CARDIOVASCULAR EVENT ASSESSMENT IN PATIENTS WITH NONOBSTRUCTIVE CORONARY ARTERY DISEASE UNDERGOING DUAL ANTIPLATELET TREATMENT**. Georgian medical news 2020:43-46.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33526728
ABSTRACT
The aim of our study was to learn the differences in baseline presentation between NObCAD and obstructive coronary artery disease (ObCAD) subjects, to compare the likelihood of several clinical outcomes and the rate of primary endpoints between this groups. Out study included 165 patients: 115 patients with NObCAD ACS, 50 - with ObCAD ACS. Inclusion criteria: age >18 year; Presence of any atherosclerotic stenosis greater than 20% but less than 50% in the left main coronary artery, and greater than 20% but less than 70% in any other major epicardial coronary artery. Patients with NObCAD ACS were randomly assign in an 1:1 ratio in 2 group: Group A (n=55) received dual antiplatelet treatment with aspirin 100-160 mg once daily and clopidogrel 75 mg once daily for three months. Group B (n=60) received only aspirin 100-160 mg once daily for three months. 50 patients with ObCAD ACS entered in group C - controlled group, patients were treated according appropriate treatment guidelines. Clinical, demographic and treatment data were investigated. Demographic variables included age and gender. Comorbidities included smoking, diabetes, hyperlipidemia, hypertension, obesity, and prior history of heart disease (angina, heart failure, myocardial infarction, coronary artery bypass grafting, and percutaneous coronary intervention), renal and liver disease. ECG changes and initial laboratory data were recorded. Laboratory analyses: CBC, urine test, serum

lipid profile, fasting blood glucose and HbA1C, creatinine and eGFR, liver enzymes were provided. All patients underwent coronary angiography. Data describing patient management included use of β-blockers, aspirin, ACE inhibitors or angiotensin receptor blockers, lipid-lowering agents. We categorized each patient by CAD extent. To accomplish this, we categorized each patient by CAD severity in a single, double, or triple-vessel distribution. Follow-up evaluations were performed at one, two and three months and 1 year. At these visits was assessed primary endpoints - MACE (Major adverse cardiac events): 1year hospitalization for Myocardial infarction or other cardiovascular causes after index angiography, cardiovascular death, revascularization, survival. We studied type and frequency of bleeding during treatment and follow up period. After data assessment we can tell, that the combination of clopidogrel and aspirin was not significantly more effective than aspirin alone in reducing the rate of myocardial infarction, but there was significant difference between groups regarding the CVD event rates, revascularization frequency and bleeding rate.

[31] *Turgay Yıldırım Ö, Kaya Ş*. **The atherogenic index of plasma as a predictor of mortality in patients with COVID-19**. Heart Lung 2021; 50:329-333.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33524862

ABSTRACT

BACKGROUND: Coronavirus disease 2019 (COVID-19) has become a global health threat, and thus, an early and effective set of predictors is needed to manage the course of the disease. OBJECTIVES: We aim to determine the effect of SARS-CoV-2 on lipid profile and to evaluate whether the atherogenic index of plasma (AIP) could be used to predict in-hospital mortality in COVID-19 patients. METHODS: In this retrospective chart review study, a total of 139 confirmed COVID-19 patients, whose diagnoses are confirmed by PCR and computerized tomography results, are enrolled. The study population is divided into two groups: the deceased patient group and the survivor group. For each patient, fasting total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and the triglyceride values are obtained from the laboratory tests required at the admission to hospital. Finally, the AIP is calculated as the base 10 logarithm of the triglyceride to HDL-C ratio. Distributional normality of the data is checked and depending on the normality of the data, either T test or Mann Whithey U test is employed to compare the two aforementioned study groups. RESULTS: Mean age of the study population is 49.2 ± 20.8 and 61.2% (n = 85) is male. Out of the 139 patients 26 have deceased and the remaining 113 patients survived the disease. Mean age of the deceased patients was 71.8*8.9 and mean age of the survivor patients is 44.0*19.2 ($p < 0.001$). The deceased group had more patients with hypertension (50.0% vs. 23.0, $p = 0.006$), diabetes mellitus (35.6% vs. 10.6%, $p = 0.002$), cardiovascular diseases (23.1% vs. 4.4%, $p = 0.001$), chronic renal insufficiency (11.5% vs. 0.9%, $p = 0.003$) and atrial fibrillation (7.7% vs 0%, $p = 0.003$). The AIP values in the deceased group are found to be statistically higher ($p < 0.001$) than the survivor group. As a measure of mortality, the area under the operating characteristic curve for the AIP is calculated as 0.850 (95% confidence interval: 0.772-0.928) along with the optimal cut-off value of 0.6285 (78.6% sensitivity and 80.5% specificity). Furthermore, the AIP value is observed to be elevated in patients with pneumonia, intubation history, and intensive care admission during hospital stay ($p = 0.002$, $p < 0.001$ and $p < 0.001$, respectively). Finally, compared to the survivor group, total cholesterol, HDL-C, LDL-C values are lower ($p = 0.004$, $p < 0.001$ and $p < 0.001$, respectively) and triglyceride levels are higher ($p < 0.001$) in deceased patients. CONCLUSION: In this study, we show that the AIP levels higher than 0.6285 can predict in-

hospital mortality for COVID-19 patients. Moreover, the AIP emerges as a good candidate to be used as an early biomarker to predict pneumonia, intubation and intensive care need. Hence, regular check of the AIP levels in COVID-19 patients can improve management of these patients and prevent deterioration of the disease.

[32] *Al-Maiahy TJ, Al-Gareeb AI, Al-Kuraishy HM*. **Role of dyslipidemia in the development of early-onset preeclampsia**. Journal of advanced pharmaceutical technology & research 2021; 12:73-78.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33532359
ABSTRACT
Preeclampsia (PE) is a gestational-related disease presented with hypertension, peripheral edema, and proteinuria after 20 weeks of gestation. In PE, there are various metabolic changes like dyslipidemia. In addition, both PE and dyslipidemia are associated with changes of platelet indices. Thus, objective of the current study was to illustrate the potential role of dyslipidemia and platelet changes in pregnant women with PE. This case-control study involved 37 preeclamptic pregnant women as compared to 24 healthy pregnant women as controls. Blood pressure profile, lipid profile, proteinuria, and platelet indices were measured. Blood pressure profile was higher in preeclamptic pregnant women as compared to the controls ($P < 0.01$). There was a significant dyslipidemic status in preeclamptic pregnant women compared with the controls ($P < 0.01$). Platetetcrit (PCT) and platelet count (PC) were lower in preeclamptic pregnant women compared with the controls ($P = 0.001$). On the other hand, platelet distribution width (PDW), mean platelet volume (MPV), and platelet-large cell ratio (P-LCR) were higher in the pregnant women with PE as compared with the controls ($P = 0.001$). PCT and PC were insignificantly linked, while P-LCR, MPV and PDW were significantly correlated with total cholesterol, triglyceride, low-density lipoprotein (LDL)/high-density lipoprotein (HDL) ratio, systolic blood pressure, DBP, and MAP in preeclamptic patients compared with women of normal pregnancy. Both dyslipidemia and alterations in the platelet indices are correlated with blood pressure profile in PE. High MPV and PDW in association with high LDL/HDL ratio in pregnant women herald risk of PE.

[33] *Al-Mashhadi RH, Al-Mashhadi AL, Nasr ZP et al.* **Local Pressure Drives Low-Density Lipoprotein Accumulation and Coronary Atherosclerosis in Hypertensive Minipigs**. Journal of the American College of Cardiology 2021; 77:575-589.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33538256
ABSTRACT
BACKGROUND: The mechanisms by which hypertension accelerates coronary artery disease are poorly understood. Patients with hypertension often have confounding humoral changes, and to date, no experimental models have allowed analysis of the isolated effect of pressure on atherosclerosis in a setting that recapitulates the dimensions and biomechanics of human coronary arteries. OBJECTIVES: This study sought to analyze the effect of pressure on coronary atherosclerosis and explore the underlying mechanisms. METHODS: Using inflatable suprarenal aortic cuffs, we increased mean arterial pressure by >30 mm Hg in the cephalad body part of wild-type and hypercholesterolemic proprotein convertase subtilisin kexin type 9 (PCSK9)(D374Y) Yucatan minipigs for >1 year. Caudal pressures remained normal. RESULTS: Under hypercholesterolemic conditions in PCSK9(D374Y) transgenic minipigs, cephalad hypertension accelerated coronary atherosclerosis to

almost 5-fold with consistent development of fibroatheromas that were sufficiently large to cause stenosis on computed tomography angiography. This was caused by local pressure forces, because vascular beds shielded from hypertension, but exposed to the same humoral factors, showed no changes in lesion formation. The same experiment was conducted under normocholesterolemic conditions in wild-type minipigs to examine the underlying mechanisms. Hypertension produced clear changes in the arterial proteome with increased abundance of mechanical strength proteins and reduced levels of infiltrating plasma macromolecules. This was paralleled by increased smooth muscle cells and increased intimal accumulation of low-density lipoproteins in the coronary arteries. CONCLUSIONS: Increased pressure per se facilitates coronary atherosclerosis. Our data indicate that restructuring of the artery to match increased tensile forces in hypertension alters the passage of macromolecules and leads to increased intimal accumulation of low-density lipoproteins.

[34] *Cicero AFG, Fogacci F, Zambon A*. **Red Yeast Rice for Hypercholesterolemia: JACC Focus Seminar**. Journal of the American College of Cardiology 2021; 77:620-628.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33538260
ABSTRACT
The extracts of red yeast rice (RYR) are currently the most effective cholesterol-lowering nutraceuticals. This activity is mainly due to monacolin K, a weak reversible inhibitor of 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase, whose daily consumption causes a reduction in low-density lipoprotein (LDL)-cholesterol plasma levels up to 15% to 25% within 6 to 8 weeks. The decrease in LDL-cholesterol is accompanied by a proportional decrease in total and non-high-density lipoprotein cholesterol, plasma apolipoprotein B, and high-sensitivity C-reactive protein. Some trials suggest that RYR use is associated with improvement in endothelial function and arterial stiffness, whereas a long-term study supports its role in the prevention of cardiovascular events. Despite the statin-like mechanism of action, the risk related to 3 to 10 mg monacolin K taken per day is minimal (mild myalgia in previously severely statin-intolerant subjects). RYR could represent a therapeutic tool to support lifestyle improvement in managing mild to moderate hypercholesterolemia in low-risk patients, including those who cannot be treated with statins or other LDL-cholesterol-lowering therapies.

[35] *Weinberg RL, Brook RD, Rubenfire M, Eagle KA*. **Cardiovascular Impact of Nutritional Supplementation With Omega-3 Fatty Acids: JACC Focus Seminar**. Journal of the American College of Cardiology 2021; 77:593-608.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33538258
ABSTRACT
Omega-3 polyunsaturated fatty acids (PUFAs) are a key component of a heart-healthy diet. For patients without clinical atherosclerotic cardiovascular disease, 2 or more servings of fatty fish per week is recommended to obtain adequate intake of omega-3 PUFAs. If this not possible, dietary supplementation with an appropriate fish oil may be reasonable. Supplementation with omega-3 PUFA capsules serves 2 distinct but overlapping roles: treatment of hypertriglyceridemia and prevention of cardiovascular events. Marine-derived omega-3 PUFAs reduce triglycerides and have pleiotropic effects including decreasing inflammation, improving plaque composition and stability, and altering cellular membranes. Clinical trial data have shown inconsistent results with omega-3 PUFAs improving cardiovascular outcomes. In this paper, the authors provide an overview of PUFAs and a

summary of key clinical trial data. Recent trial data suggest the use of prescription eicosapentaenoic acid ethyl ester for atherosclerotic cardiovascular disease event reduction in selected populations.

[36] *Doi T, Hori M, Harada-Shiba M et al.* **Patients With LDLR and PCSK9 Gene Variants Experienced Higher Incidence of Cardiovascular Outcomes in Heterozygous Familial Hypercholesterolemia**. Journal of the American Heart Association 2021:e018263.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33533259

ABSTRACT

Background Patients with familial hypercholesterolemia who harbored both low-density lipoprotein receptor (LDLR) and PCSK9 (proprotein convertase subtilisin/kexin type 9) gene variants exhibit severe phenotype associated with substantially high levels of low-density lipoprotein cholesterol. In this study, we investigated the cardiovascular outcomes in patients with both LDLR and PCSK9 gene variants. Methods and Results A total of 232 unrelated patients with LDLR and/or PCSK9 gene variants were stratified as follows: patients with LDLR and PCSK9 (LDLR/PCSK9) gene variants, patients with LDLR gene variant, and patients with PCSK9 gene variant. Clinical demographics and the occurrence of primary outcome (nonfatal myocardial infarction) were compared. The observation period of primary outcome started at the time of birth and ended at the time of the first cardiac event or the last visit. Patients with LDLR/PCSK9 gene variants were identified in 6% of study patients. They had higher levels of low-density lipoprotein cholesterol (P=0.04) than those with LDLR gene variants. On multivariate Cox regression model, they experienced a higher incidence of nonfatal myocardial infarction (hazard ratio, 4.62; 95% CI, 1.66-11.0; P=0.003 versus patients with LDLR gene variant). Of note, risk for nonfatal myocardial infarction was greatest in male patients with LDLR/PCSK9 gene variants compared with those with LDLR gene variant (86% versus 24%; P<0.001). Conclusions Patients with LDLR/PCSK9 gene variants were high-risk genotype associated with atherogenic lipid profiles and worse cardiovascular outcomes. These findings underscore the importance of genetic testing to identify patients with LDLR/PCSK9 gene variants, who require more stringent antiatherosclerotic management.

[37] *Cordero A, Rodríguez-Mañero M, Fácila L et al.* **Prevention of myocardial infarction and stroke with PCSK9 inhibitors treatment: a metanalysis of recent randomized clinical trials**. Journal of diabetes and metabolic disorders 2020; 19:759-765.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33520801

ABSTRACT

PURPOSE: Proprotein convertase subtilisin/kexin 9 (PCSK9) inhibitors treatment induce large reductions in low-density lipoprotein cholesterol (LDLc) and major cardiovascular events. Clinical trials might have been underpowered to test the effect of PSCK9 inhibitors treatment on myocardial infarction and stroke, two of the most relevant cardiovascular events, since all analyzed a combined endpoint. METHODS: we performed a meta-analysis, with currently available studies involving PCSK9 inhibitors and event rate adjudication, with the aim of assessing treatment effects on myocardial infarction and stroke. RESULTS: We included 81,700 patients, 41,979 treated with a PSCK9 inhibitors: 17,244 with evolocumab; 13,720 with bococizumab and 11,015 with alirocumab. A total of 1,319 cases of myocardial infarctions were registered in the treatment group vs. 1,608 in controls, resulting in 19.0% reduction associated with PCSK9 treatment (RR: 0.81, 95% CI 0.76-0.87). Similarly, PCSK9 inhibitors treatment resulted in a 25% reduction of stroke (RR: 0.75, 95% CI

0.65-0.85) when all studies were analyzed together and the statistically significant heterogeneity was not observed in the analysis restricted to end-point based clinical trials. PCSK9 inhibitors treatment had no effect on mortality (RR: 0.95, 95% CI 0.86-1.04). CONCLUSIONS: PCSK9 inhibitors reduce the incidence of myocardial infarction by 19% and stroke by 25%.

[38] *Hasanzad M, Sarhangi N, Nikfar S et al.* **A narrative review of current trends in liraglutide: insights into the unmet needs in management of type 2 diabetes and obesity**. Journal of diabetes and metabolic disorders 2020; 19:1863-1872.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33520865
ABSTRACT
Liraglutide is a long-acting human glucagon-like peptide-1 (GLP-1) analogue and an effective treatment for patients with metabolic diseases including type 2 diabetes mellitus (T2DM) and obesity. This review focuses on the mechanism of action of liraglutide as a well-known glucagon-like peptide-1 receptor agonist (GLP-1 RA) in patients with T2DM and obesity. The lower and the higher doses of GLP-1 RAs are used for glycaemic control in T2DM and in obesity respectively. GLP-1 RAs such as liraglutide enhance insulin secretion and inhibit glucagon release via the stimulation of glucagon-like peptide-1 receptors (GLP-1Rs). Liraglutide decreases hemoglobin A1c (HbA1c) in type 2 diabetes (T2D) patients when prescribes as monotherapy or in combination with one or more antidiabetic drugs. Usually, it is well tolerated with minor hypoglycemia in combination therapy. Liraglutide reduces cardiovascular events and related risk factors including improvement of lipid profile and control of blood pressure. Accordingly, it can be cost-effective and may be a budget neutral medication option by considering its protective effect on the cardiovascular system in long-term use in the health care plan. In the near future, by pharmacogenomics approach, prediction of the highest patient's response with the lowest adverse drug reactions and also rationality of drug development will be possible. Liraglutide can be used as a desirable medicine for glycemic control and obesity. It shows extensive evidence based benefits in diabetes complications. In this narrative review, we have summarized and evaluated studies related to the role of liraglutide in clinical practice.

[39] *Koo BK, Park S, Han KD, Moon MK*. **Hypertriglyceridemia Is an Independent Risk Factor for Cardiovascular Diseases in Korean Adults Aged 30-49 Years: a Nationwide Population-Based Study**. J Lipid Atheroscler 2021; 10:88-98.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33537256
ABSTRACT
OBJECTIVE: This study was conducted to estimate the incidence of cardiovascular disease (CVD) independently from low-density lipoprotein (LDL) cholesterol according to triglyceride (TG) levels in young adults. METHODS: Subjects aged 30-49 years with data from routine health check-ups provided by the National Health Insurance Service during 2009 were selected. The primary outcome was incident CVD, defined as a composite of ischemic heart disease and ischemic stroke during the follow-up period from 2009 to 2018. RESULTS: The mean age of study subjects (n=1,823,537) was 40.1±5.7 years, and the median follow-up period was 8.3 years. The quartiles of serum TG levels at the baseline were calculated: Q1, <74 mg/dL; Q2, 74-108 mg/dL; Q3, 109-166 mg/dL; and Q4: >166 mg/dL. The highest quartile of TG levels (Q4) had a significantly higher risk of the primary outcome than Q1 (hazard ratio [HR], 2.40 [95% confidence interval; CI, 2.33-2.47]). Q2 and Q3 also experienced the primary outcome more frequently than Q1 (HR, 1.37 [95% CI, 1.33-1.42] and HR,

1.80 [95% CI, 1.75-1.86], respectively). Even after adjustment for age, sex, obesity, alcohol drinking amount, smoking, LDL cholesterol, diabetes mellitus, hypertension, lipid-lowering medication use, and family history of CVD, there was a significant dose-response relationship between TG quartiles and the risk of the primary outcome (HR per quartile, 1.13 [95% CI, 1.12-1.14]). CONCLUSION: In conclusion, in the Korean population aged 30-49 years, high TG levels independently increased future CVD risk in both men and women.

[40] *Yang Y, Han K, Park SH et al.* **High-Density Lipoprotein Cholesterol and the Risk of Myocardial Infarction, Stroke, and Cause-Specific Mortality: a Nationwide Cohort Study in Korea**. J Lipid Atheroscler 2021; 10:74-87.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33537255
ABSTRACT
OBJECTIVE: We aimed to investigate the relationship between high-density lipoprotein cholesterol (HDL-C) level and the risk of myocardial infarction (MI), stroke, and cause-specific mortality. METHODS: Using the Korean National Health Insurance Service-National Sample Cohort, we identified 343,687 subjects (men, 176,243; women, 167,444) aged ≥20 years who underwent health examinations between 2009 and 2012. HDL-C levels were categorized based on the concentration with 10 mg/dL intervals, starting from levels <30 mg/dL, with levels ≥90 mg/dL considered the highest. The endpoints of the study were newly-diagnosed MI, stroke, or mortality. We used the Cox proportional hazards model with restricted cubic splines. RESULTS: During a median follow-up of 6.0 years, the number of cases of death, MI, and stroke were 6,617, 4,064, and 3,435 in men and 3,677, 2,804, and 2,891 in women, respectively. The risk of all-cause mortality, cancer mortality, other mortality, and stroke was the lowest at HDL-C concentrations of 57-76 mg/dL in the spline curves; inverse associations with increased risk were observed at the lower HDL-C levels. In contrast, the lowest risk of cardiovascular mortality and MI was observed at the extreme high end. In men, there was a significant inverse and graded increase in hazard ratios of all outcomes in the lower HDL-C categories compared to the reference group (50-59 mg/dL). In the higher HDL-C categories, no significant increase in outcomes was observed. Women showed similar trends. CONCLUSION: The risk of mortality, MI, and stroke was high at low HDL-C levels in the Korean general population. However, extremely high HDL-C levels were not associated with an increased risk of mortality, MI, and stroke.

[41] *Hu Y, Meuret C, Martinez A et al.* **Distinct patterns of apolipoprotein C-I, C-II, and C-III isoforms are associated with markers of Alzheimer's disease**. Journal of lipid research 2020; 62:100014.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33518512
ABSTRACT
Apolipoproteins C-I, C-II, and C-III interact with ApoE to regulate lipoprotein metabolism and contribute to Alzheimer's disease pathophysiology. In plasma, apoC-I and C-II exist as truncated isoforms, while apoC-III exhibits multiple glycoforms. This study aimed to 1) delineate apoC-I, C-II, and C-III isoform profiles in cerebrospinal fluid (CSF) and plasma in a cohort of nondemented older individuals (n = 61), and 2) examine the effect of APOE4 on these isoforms and their correlation with CSF Aβ42, a surrogate of brain amyloid accumulation. The isoforms of the apoCs were immunoaffinity enriched and measured with MALDI-TOF mass spectrometry, revealing a significantly

higher percentage of truncated apoC-I and apoC-II in CSF compared with matched plasma, with positive correlation between CSF and plasma. A greater percentage of monosialylated and disialylated apoC-III isoforms was detected in CSF, accompanied by a lower percentage of the two nonsialylated apoC-III isoforms, with significant linear correlations between CSF and plasma. Furthermore, a greater percentage of truncated apoC-I in CSF and apoC-II in plasma and CSF was observed in individuals carrying at least one APOE Ɛ4 allele. Increased apoC-I and apoC-II truncations were associated with lower CSF Aβ42. Finally, monosialylated apoC-III was lower, and disialylated apoC-III greater in the CSF of Ɛ4 carriers. Together, these results reveal distinct patterns of the apoCs isoforms in CSF, implying CSF-specific apoCs processing. These patterns were accentuated in APOE Ɛ4 allele carriers, suggesting an association between APOE4 genotype and Alzheimer's disease pathology with apoCs processing and function in the brain.

[42] *Akbar MIA, Yosediputra A, Pratama RE et al.* **Pravastatin suppresses inflammatory cytokines and endothelial activation in patients at risk of developing preeclampsia: INOVASIA 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 2021:1-8.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33522342

ABSTRACT

INTRODUCTION: The Indonesian INOVASIA study is an ongoing multicentre randomized, open controlled trial of pravastatin for the prevention of preeclampsia in patients deemed to be high risk. Here we evaluate the effects of pravastatin on circulating inflammatory and endothelial markers, i.e. Vascular Endothelial Growth Factor (VEGF), Interleukin-6 (IL-6), Endothelin-1 (ET-1), and Nitric Oxide (NO). METHODS: Pregnant women deemed to be at a high risk of developing preeclampsia women were recruited based on the Fetal Medicine Foundation preeclampsia screening test or a history of preterm preeclampsia, or clinical risk factors in combination with an abnormal uterine artery Doppler flow pattern at 11-20 week's gestation. This is a nested cohort study within the larger trial (INOVASIA); 38 patients were consecutively recruited and assigned to the pravastatin group and the control group. Participants in the pravastatin group received pravastatin (2 × 20 mg p.o) in addition to a standard regimen of aspirin (80 mg p.o) and calcium (1 g p.o), from 14 to 20 weeks until delivery. Blood samples to measure the various biomarkers were obtained in consecutive patients before starting the research medication and just before delivery (pre and post-test examination). RESULT: The number of samples on the 2 time points for the various biomarkers was: VEGF: 38, IL-6: 30, ET-1: 38, and NO: 35. IL-6 levels decreased significantly in the pravastatin group (mean ± SD): (191.87 ± 82.99 vs. 151.85 + 48.46, p = .013), while levels in the control group did not change significantly (median (interquartile range)) (144.17 (53.91) vs. 140.82 (16.18), p = .177). ET-1 levels decreased significantly in the pravastatin group (3.64 ± 0.85 vs. 3.01 ± 0.74, p = .006) while the control group had more or less stable levels (3.57 ± 1.12 vs. 3.78 ± 0.73 p = .594). NO was the only serum marker that showed significant changes in both groups. NO levels increased in pravastatin group (11.30 (17.43) vs. 41.90 (53.18), p = .044) and decreased in control group (38.70 (34.80) vs. 10.03 (26.96), p = .002). VEGF levels appeared to follow opposite trends in the 2 groups (NS) (Pravastatin: 3.22 (0.62) vs. 3.28 (0.75), p = .402. Control: 3.38 (0.83) vs. 3.06 (0.74), p = .287). CONCLUSION: Administration of 40 mg pravastatin resulted in an improvement in NO levels, and a decrease in IL-6

and endothelin (ET-1) levels. The direction of the effect of pravastatin on these biomarkers appears to underpin the potential for a beneficial effect of pravastatin in the prevention of preeclampsia.

[43] *Dundua DP, Strazhesko ID*. **[Detection of peripheral artery disease in patients with ischemic heart disease. A quick guide for medical practitioners]**. Kardiologiia 2021; 60:125-132.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33522477

ABSTRACT

In this manual, the authors focused on the principal methods for diagnosis of peripheral artery disease in cardiological patients, from the interview and physical examination to functional tests and vascular visualization. Diagnostic and prognostic value of each method, its potentialities for reducing the risk of cardiovascular events (CVE), including myocardial infarction (MI), ischemic stroke (IS) or extremity amputation in critical ischemia, and overall mortality are discussed. The authors provided current information about a possibility of reducing the risk of CVE by intensifying the antithrombotic therapy according to results of the COMPASS study.

[44] *Merkulova IN, Shariya MA, Mironov VM et al.* **[Computed Tomography Coronary Angiography Possibilities in "High Risk" Plaque Identification in Patients with non-ST-Elevation Acute Coronary Syndrome: Comparison with Intravascular Ultrasound]**. Kardiologiia 2021; 60:64-75.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33522469

ABSTRACT

Aim To evaluate structural characteristics of atherosclerotic plaques (ASP) by coronary computed tomography arteriography (CCTA) and intravascular ultrasound (IVUS).Material and methods This study included 37 patients with acute coronary syndrome (ACS). 64-detector-row CCTA, coronarography, and grayscale IVUS were performed prior to coronary stenting. The ASP length and burden, remodeling index (RI), and known CT signs of unstable ASP (presence of dot calcification, positive remodeling of the artery in the ASP area, irregular plaque contour, presence of a peripheral high-density ring and a low-density patch in the ASP). The ASP type and signs of rupture or thrombosis were determined by IVUS.Results The IVUS study revealed 45 unstable ASP (UASP), including 25 UASP with rupture and 20 thin-cap fibroatheromas (TCFA), and 13 stable ASP (SASP). No significant differences were found between distribution of TCFA and ASP with rupture among symptom-associated plaques (SAP, n=28) and non-symptom-associated plaques (NSAP, n=30). They were found in 82.1 and 73.3% of cases, respectively (p>0.05), which indicated generalization of the ASP destabilization process in the coronary circulation. However, the incidence of mural thrombus was higher for SAP (53.5 and 16.6% of ASP, respectively; p<0.001). There was no difference between UASP and SASP in the incidence of qualitative ASP characteristics or in values of quantitative ASP characteristics, including known signs of instability, except for the irregular contour, which was observed in 92.9% of UASP and 46.1% of SASP (p=0.0007), and patches with X-ray density ≤46 HU, which were detected in 83.3% of UASP and 46.1% of SASP (p=0.01). The presence of these CT criteria 11- and 7-fold increased the likelihood of unstable ASP (odd ratio (OR), 11.1 at 95% confidence interval (CI), from 2.24 to 55.33 and OR, 7.0 at 95% CI, from 5.63 to 8.37 for the former and the latter criterion, respectively).Conclusion According to IVUS data, two X-ray signs are most characteristic for UASP, the irregular contour and a patch with X-ray density ≤46 HU. The presence of these signs 11- and 7-fold, respectively, increases the likelihood of unstable ASP.

[45] *Dehghan A, Vasan SK, Fielding BA, Karpe F*. **A prospective study of the relationships between change in body composition and cardiovascular risk factors across the menopause**. Menopause (New York, N.Y.) 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33534433
ABSTRACT
OBJECTIVE: Menopause increases the risk of cardiovascular disease (CVD) which in part has been attributed to the rise in cholesterol and blood pressure (BP). This study examined the hypothesis that menopausal changes in body composition and regional fat depots relate to the change in CVD risk factors. METHODS: A prospective recall study was designed to capture premenopausal women to be re-examined soon after menopause. A total of 97 women from the Oxford Biobank underwent dual x-ray absorptiometry, blood biochemistry, and BP readings pre- and postmenopause. RESULTS: Despite minimal changes in body weight over the 5.1±0.9 year follow-up period, there was an increase in total fat mass and a decline in lean mass, where the proportional change of regional fat mass was the greatest for the visceral fat depot (+22%, P<0.01). Plasma ApoB (+12%, P<0.01) and C-reactive protein (+45%, P<0.01) increased as did systolic (+7%, P<0.001) and diastolic BP (+5%, P<0.001). Plasma nonesterified fatty acids decreased (-20%, P<0.05) which may reflect on a change in adipose tissue function across the menopause. PCSK-9 decreased (-26%, P<0.01) which suggests a compensation for the postmenopausal reduction in low-density lipoprotein receptor activity. Using multilinear regression analyses the changes in ApoB and diastolic BP were associated with visceral fat mass change, but this association was lost when adjusted for total fat mass change. CONCLUSION: The increase in CVD risk factor burden across menopause may not be driven by changes in body composition, rather by functional changes in end organs such as adipose tissue and liver.

[46] *Szekeres Z, Toth K, Szabados E*. **The Effects of SGLT2 Inhibitors on Lipid Metabolism**. Metabolites 2021; 11.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33535652
ABSTRACT
Sodium glucose co-transporter 2 (SGLT2) inhibitors are effective antihyperglycemic agents by inhibiting glucose reabsorption in the proximal tubule of the kidney. Besides improving glycemic control in patients with type 2 diabetes, they also have additional favorable effects, such as lowering body weight and body fat. Several clinical studies have demonstrated their positive effect in reducing cardiovascular morbidity and mortality. Furthermore, the use of SGLT2 inhibitors were associated with fewer adverse renal outcomes comparing to other diabetic agents, substantiating their renoprotective effect in diabetic patients. SGLT2 inhibitors have also remarkable effect on lipid metabolism acting at different cellular levels. By decreasing the lipid accumulation, visceral and subcutaneous fat, they do not only decrease the body weight but also change body composition. They also regulate key molecules in lipid synthesis and transportation, and they affect the oxidation of fatty acids. Notably, they shift substrate utilization from carbohydrates to lipids and ketone bodies. In this review we intended to summarize the role of SGLT2 inhibitors in lipid metabolism especially on lipoprotein levels, lipid regulation, fat storage and substrate utilization.

[47] *He D, Fan F, Jia J et al.* **Lipid profiles and the risk of new-onset hypertension in a Chinese community-based cohort**. Nutrition, metabolism, and cardiovascular diseases : NMCD 2020.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33549431

ABSTRACT

BACKGROUND AND AIMS: Dyslipidemia and hypertension, key risk factors for cardiovascular disease, may share similar pathophysiological processes. A longitudinal association was reported between dyslipidemia and new-onset hypertension, but few data were published in Asian. We aimed to investigate the association of lipid profiles with new-onset hypertension in a Chinese community-based non-hypertensive cohort without lipid-lowering treatment (n = 1802). METHODS AND RESULTS: New-onset hypertension was defined as any self-reported history of hypertension, systolic blood pressure ≥140 mmHg, or diastolic blood pressure ≥90 mmHg, or receiving antihypertensive medications at follow-up. Logistic regression models were used to evaluate the associations. Participants were aged 53.97 ± 7.49 years, 31.19% were men, and 64.54% with dyslipidemia. During a median of 2.30 years follow-up, the incidence of new-onset hypertension was 12.99%. Multivariate adjusted risks of new-onset hypertension increased with triglyceride increases (odds ratio [OR] = 1.14, 95% confidence interval [CI]: 1.03-1.27) and high-density lipoprotein cholesterol (HDL-C) decreases (OR = 0.47, 95% CI: 0.29-0.76) for one unit. However, threshold effects were observed for total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and non-HDL-C. Compared with subjects with hyperlipidemia, in those with normal concentrations of TC, LDL-C, and non-HDL-C increased risks of new-onset hypertension were observed with OR (95% CI) of 1.65 (1.10-2.46), 1.58 (1.07-2.33), and 1.57 (1.15-2.15) for one unit increasement, respectively, after adjusting for all covariates. CONCLUSION: Higher TG and lower HDL-C increased the risk of new-onset hypertension, but for TC, LDL-C and non-HDLC, the risk of new-onset hypertension was increased only at normal concentrations in a Chinese community-based cohort.

[48] *Ress C, Dobner J, Rufinatscha K et al.* **Apolipoprotein A5 controls fructose-induced metabolic dysregulation in mice**. Nutrition, metabolism, and cardiovascular diseases : NMCD 2020.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33549451

ABSTRACT

BACKGROUND AND AIMS: Western dietary habits are partially characterized by increased uptake of fructose, which contributes to metabolic dysregulation and associated liver diseases. For example, a diet enriched with fructose drives insulin resistance and non-alcoholic fatty liver disease (NAFLD). The molecular hubs that control fructose-induced metabolic dysregulation are poorly understood. Apolipoprotein A5 (apoA5) controls triglyceride metabolism with a putative role in hepatic lipid deposition. We explored apoA5 as a rheostat for fructose-induced hepatic and metabolic disease in mammals. METHODS AND RESULTS: ApoA5 knock out (-/-) and wildtype (wt) mice were fed with high fructose diet or standard diet for 10 weeks. Afterwards, we conducted a metabolic characterization by insulin tolerance test as well as oral glucose tolerance test. Additionally, hepatic lipid content as well as transcription patterns of key enzymes and transcription factors in glucose and lipid metabolism were evaluated. Despite comparable body weight, insulin sensitivity was significantly improved in high fructose diet fed apoA5 (-/-) when compared to wildtype mice on the same diet. In parallel, hepatic triglyceride content was significantly lower in apoA5 (-/-) mice than in wt mice. No difference was seen between apoA5 (-/-) and wt mice on a standard diet. CONCLUSION: ApoA5 is involved in fructose-induced metabolic dysregulation and associated hepatic steatosis suggesting that apoA5 may be a novel target to treat metabolic diseases.

[49] *Rodríguez-Borjabad C, Narveud I, Christensen JJ et al.* **Dietary intake and lipid levels in Norwegian and Spanish children with familial hypercholesterolemia**. Nutrition, metabolism, and cardiovascular diseases : NMCD 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33549456
ABSTRACT
BACKGROUND AND AIMS: Both the Nordic and Mediterranean diets claim to have a beneficial effect on lipid metabolism and cardiovascular prevention. The objective of this study was to compare diets consumed by children with FH at the time of diagnosis in Norway and Spain and to study their relationship with the lipid profile. METHODS AND RESULTS: In this cross-sectional study, we appraised the dietary intake in children (4-18 years old) with (n = 114) and without FH (n = 145) from Norway and Spain. We compared Nordic and Mediterranean diet composition differences and determined the association between food groups and lipid profiles. RESULTS: The Spanish FH group had a higher intake of total fats (mainly monounsaturated fatty acids (MUFAs)), cholesterol and fibre, but a lower intake of polyunsaturated fatty acids (PUFAs) compared to the Norwegian FH group. The Norwegian children consumed more rapeseed oil, low-fat margarine and whole grains and less olive oil, eggs, fatty fish, meat, legumes and nuts. In the Norwegian FH group, fat and MUFAs were directly correlated with total cholesterol, low-density lipoprotein cholesterol and apolipoprotein B and inversely correlated with high-density lipoprotein (HDL-C). In Spanish children with FH, the intake of fats (mainly MUFAs) was directly associated with HDL-C and apolipoprotein A1. CONCLUSIONS: Despite a similar lipid phenotype, diets consumed by children with FH in Norway and Spain have significant differences at time of diagnosis. Nutrition advice should be more adapted to local intake patterns than on specific nutrient composition.

[50] *Scicali R, Di Pino A, Urbano F et al.* **Analysis of steatosis biomarkers and inflammatory profile after adding on PCSK9 inhibitor treatment in familial hypercholesterolemia subjects with nonalcoholic fatty liver disease: A single lipid center real-world experience**. Nutrition, metabolism, and cardiovascular diseases : NMCD 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33549441
ABSTRACT
BACKGROUND AND AIMS: Nonalcoholic fatty liver disease (NAFLD) may be crucial in subjects with familial hypercholesterolemia (FH). We aimed to evaluate the effect of the inhibitors of proprotein convertase subtilisin/kexin type 9 (PCSK9-i) on steatosis biomarkers such as triglyceride-glucose index (TyG) and hepatic steatosis index (HSI) and analyse the role of TG/HDL in this population before and after adding-on PCSK9-i. METHODS AND RESULTS: In this observational study, we evaluated 26 genetically confirmed FH patients with NAFLD and an LDL-C off-target despite high-intensity statins plus ezetimibe. All patients added PCSK9-i treatment and obtained biochemical analysis and TyG and HSI evaluation at baseline and after six months of PCSK9-i. No difference of steatosis biomarkers was found after adding-on PCSK9-i therapy. In a secondary analysis, we divided the study population in two groups according to TG/HDL median value: high TG/HDL group (H-TG/HDL) and low TG/HDL group (L-TG/HDL). TyG and HSI were significantly lower in the L-TG/HDL than H-TG/HDL group (for TyG 9.05 ± 0.34 vs 9.51 ± 0.32; for HSI 38.43 ± 1.35 vs 41.35 ± 1.83, p value for both < 0.05). After six months of PCSK9-i therapy, TyG and HSI were significantly reduced in the L-TG/HDL group after PCSK9-i therapy (-7.5% and -8.4% respectively, p value for both < 0.05) and these biomarkers were lower compared to H-TG/HDL group (for TyG

8.37 ± 0.14 vs 9.19 ± 0.12; for HSI 35.19 ± 1.32 vs 39.48 ± 1.33, p value for both < 0.05). CONCLUSION: In conclusion, PCSK9-i therapy significantly ameliorate steatosis biomarkers in FH patients with low TG/HDL; our results appear to be consistent with a beneficial role of PCSK9-i on steatosis biomarkers in FH subjects with NAFLD.

[51] *Zeller M, Lambert G, Farnier M et al.* **PCSK9 levels do not predict severity and recurrence of cardiovascular events in patients with acute myocardial infarction**. Nutrition, metabolism, and cardiovascular diseases : NMCD 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33546945
ABSTRACT
BACKGROUND AND AIMS: It remains unclear whether serum PCSK9 levels can predict the severity of the disease and the risk of future events in patients with coronary artery disease (CAD). We aimed to evaluate the association between PCSK9 levels, metabolic parameters, severity of CAD on coronary angiography (SYNTAX score), and the risk of in-hospital events and at one-year follow-up. METHODS AND RESULTS: From September 2015 to December 2016, serum PCSK9 levels were measured on admission in patients not previously receiving statin therapy, and admitted for an acute myocardial infarction (MI), in an intensive care unit from a university hospital. In a total of 648 patients (mean age: 66 years, 67% male), median PCSK9 was 263 ng/ml, higher for females compared with males (270 vs 256 ng/ml, p = 0.009). Serum PCSK9 was associated with LDL cholesterol (r = 0.083, p = 0.036), total cholesterol (r = 0.136, p = 0.001) and triglycerides (r = 0.137, p = 0.001). A positive association was also observed in the subgroup of patients with CRP >10 mg/L (p < 0.001), but not with NT-proBNP, troponin and creatine kinase. PCSK9 levels were similar whatever the SYNTAX score or the number of significant coronary lesions. PCSK9 levels were not associated with in-hospital events (death, recurrent MI and stroke) and events (cardiovascular death, cardiovascular events, recurrent MI) at one-year follow-up. CONCLUSIONS: In this large cohort of patients hospitalized for acute MI and not previously receiving statin therapy, PCSK9 levels was not associated with the severity or the recurrence of cardiovascular events. The clinical utility of measuring PCSK9 levels for this category of patients therefore appears limited.

[52] *Lancellotti P, Ancion A, Scheen AJ*. **[Fixed combination atorvastatin-perindopril (Lipercosyl®) for substitution treatment of cardiovascular risk management]**. Revue medicale de Liege 2021; 76:128-133.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33543860
ABSTRACT
Fixed combination atorvastatin-perindopril (Lipercosyl®) for substitution treatment of cardiovascular risk management Lipercosyl® is a fixed combination of atorvastatin and perindopril, a cholesterol-lowering and an antihypertensive agent, which allows blood pressure and cholesterol levels to be controlled in hypertensive patients with dyslipidemia : atorvastatin, an inhibitor of HMG-CoA reductase, and perindopril, an angiotensin converting enzyme inhibitor. Six presentations with different dosages of each molecule are available so the treatment can be individualized. Specific precautions of use to each medication must obviously be observed. The use of such a combination helps to ensure a good level of cholesterol while controlling blood pressure.

[53] *Caterino M, Gelzo M, Sol S et al.* **Dysregulation of lipid metabolism and pathological inflammation in patients with COVID-19**. Scientific reports 2021; 11:2941.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33536486

ABSTRACT

In recent months, Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread throughout the world. COVID-19 patients show mild, moderate or severe symptoms with the latter ones requiring access to specialized intensive care. SARS-CoV-2 infections, pathogenesis and progression have not been clearly elucidated yet, thus forcing the development of many complementary approaches to identify candidate cellular pathways involved in disease progression. Host lipids play a critical role in the virus life, being the double-membrane vesicles a key factor in coronavirus replication. Moreover, lipid biogenesis pathways affect receptor-mediated virus entry at the endosomal cell surface and modulate virus propagation. In this study, targeted lipidomic analysis coupled with proinflammatory cytokines and alarmins measurement were carried out in serum of COVID-19 patients characterized by different severity degree. Serum IL-26, a cytokine involved in IL-17 pathway, TSLP and adiponectin were measured and correlated to lipid COVID-19 patient profiles. These results could be important for the classification of the COVID-19 disease and the identification of therapeutic targets.

[54] *Peymani P, Dehesh T, Aligolighasemabadi F et al.* **Statins in patients with COVID-19: a retrospective cohort study in Iranian COVID-19 patients**. Transl Med Commun 2021; 6:3.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33521322

ABSTRACT

BACKGROUND: The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has profoundly affected the lives of millions of people. To date, there is no approved vaccine or specific drug to prevent or treat COVID-19, while the infection is globally spreading at an alarming rate. Because the development of effective vaccines or novel drugs could take several months (if not years), repurposing existing drugs is considered a more efficient strategy that could save lives now. Statins constitute a class of lipid-lowering drugs with proven safety profiles and various known beneficial pleiotropic effects. Our previous investigations showed that statins have antiviral effects and are involved in the process of wound healing in the lung. This triggered us to evaluate if statin use reduces mortality in COVID-19 patients. RESULTS: After initial recruitment of 459 patients with COVID-19 (Shiraz province, Iran) and careful consideration of the exclusion criteria, a total of 150 patients, of which 75 received statins, were included in our retrospective study. Cox proportional-hazards regression models were used to estimate the association between statin use and rate of death. After propensity score matching, we found that statin use appeared to be associated with a lower risk of morbidity [HR = 0.85, 95% CI = (0.02, 3.93), P = 0.762] and lower risk of death [(HR = 0.76; 95% CI = (0.16, 3.72), P = 0.735)]; however, these associations did not reach statistical significance. Furthermore, statin use reduced the chance of being subjected to mechanical ventilation [OR = 0.96, 95% CI = (0.61-2.99), P = 0.942] and patients on statins showed a more normal computed tomography (CT) scan result [OR = 0.41, 95% CI = (0.07-2.33), P = 0.312]. CONCLUSIONS: Although we could not demonstrate a significant association between statin use and a reduction in mortality in patients with COVID19, we do feel that our results are promising and of clinical relevance and warrant the need for prospective randomized controlled trials and extensive retrospective studies to further evaluate and validate the potential

beneficial effects of statin treatment on clinical symptoms and mortality rates associated with COVID-19.