[1] *Yan P, Xu Y, Miao Y et al.* **Association of remnant cholesterol with chronic kidney disease in middle-aged and elderly Chinese: a population-based study**. Acta diabetologica 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34181081

ABSTRACT

AIMS: Limited data regarding the association between remnant cholesterol (RC) and chronic kidney disease (CKD), largely based on an estimated glomerular filtration rate (eGFR) of<60 mL/min/1.73 m(2) (low eGFR), have yielded inconsistent results, and no report has demonstrated the relationship of RC with CKD [defined as low eGFR and/or albuminuria (defined as urinary albumin-to-creatinine ratio (ACR)≥30 mg/g)] in Chinese general middle-aged and elderly population. Hence, we aimed to investigate the association between RC and CKD in such population. METHODS: In total, 7356 Chinese participants aged≥40 years were recruited from five regional communities in Luzhou city between May 2011 and December 2011. Fasting RC was calculated from the lipid profile measured by standard laboratory procedures. Multivariate logistic regression models were used to evaluate the possible association between RC and CKD. RESULTS: Participants in the highest quartile of RC had higher body mass index, systolic and diastolic blood pressure, total cholesterol, triglyceride, low-density lipoprotein cholesterol (LDL-C), fasting and 2-h postload blood glucose, glycated hemoglobin A1C, prevalence of prediabetes, type 2 diabetes mellitus (T2DM), hypertension, CKD, albuminuria, low eGFR, and lower high-density lipoprotein cholesterol (HDL-C) and eGFR compared with those in the lowest quartile (all P for trend<0.01). Multivariate logistic regression analysis demonstrated that the risk of CKD gradually increased across RC quartiles (P for trend<0.01), and participants in the highest quartile of RC were at a significantly increased risk of prevalent CKD compared to those in the lowest quartile in total subjects (odds rate: 1.344, 95% confidence intervals 1.097-1.648, P<0.01). In subgroup analysis, significant relation between RC level and increased risk of prevalent CKD was detected in women, subjects with overweight/obesity, non-prediabetes, hypertension, normal HDL-C, appropriate and high LDL-C, and without cardiovascular disease (CVD) events after multiple adjustments. CONCLUSIONS: Higher RC is independently associated with increased risk of prevalent CKD, and RC might serve as a new risk biomarker for CKD in a general middle-aged and elderly Chinese population, especially in women, subjects with overweight/obesity, non-prediabetes, hypertension, normal HDL-C, appropriate and high LDL-C, and without CVD events.

[2] *Wang Y, Du X, Zhao R et al.* **Association of APOE polymorphisms with lipid-lowering efficacy of statins in atherosclerotic cardiovascular diseases**. Ann Acad Med Singap 2021; 50:474-480.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34195754

ABSTRACT

INTRODUCTION: The apolipoprotein E (APOE) gene is a promising candidate for the diagnosis of hyperlipoproteinaemia and atherosclerosis. Polymorphisms in APOE have been reported to result in differential efficacies of statin drugs in atherosclerotic cardiovascular disease. METHODS: We classified the APOE genotypes of 225 patients treated with atorvastatin, and analysed the relation between genotypes and serum lipid levels. RESULTS: The baseline serum levels of total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) were significantly lower in carriers of APOE ε3 than of APOE ε4 genotypes. The serum levels of TC and LDL-C decreased significantly after 1 month of atorvastatin treatment. Atorvastatin has a higher significant effect in reducing serum TC and LDL-C

levels in patients with the APOE ε4 genotype. CONCLUSION: Polymorphism in the APOE gene is related to the efficacy of atorvastatin in reducing the serum levels of TC and LDL-C.

[3] *Paraskevas KI, Nicolaides AN, Suri JS, Saba L*. **Identifying the Vulnerable Carotid Atherosclerotic Plaque in Patients With Asymptomatic Carotid Stenosis**. Angiology 2021:33197211028416.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34212770
ABSTRACT

[4] *Marcinkiewicz A, Śliż DI, Olejniczak D et al.* **Dyslipidaemia, carbohydrate metabolism disorders and arterial hypertension detected in academic employees during examinations in occupational medicine**. Ann Agric Environ Med 2021; 28:314-318.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34184516
ABSTRACT
INTRODUCTION: Many people have CVD risk factors without realising it and it is important to recognise the risk factors as soon as possible. Periodic examinations are a mandatory form of control for all employes in Poland. They provide an excellent opportunity to screen for the most common civilization diseases in the population. OBJECTIVE: The aim of this study is to evaluate the prevalence of dyslipidaemia, hyperglycaemia and hypertension among academics in a Polish university, and to compare the results between postdoctoral fellows and other academics. MATERIAL AND METHODS: The study group were postdoctoral fellows (HAB; N=135, 53 females) and other academics (NHAB; N=286, 179 females) over the age of 40 who reported for a periodic occupational medical check-up. Fasting blood samples were drawn, serum glucose, lipids and blood pressure (BP) were measured. RESULTS: The mean age was 56.7 (SD 9.8) in HAB and 49.8 (SD 8.1) in NHAB. Mean systolic BP and glycaemia were significantly higher in male HAB group than male NHAB (135.8 vs 130.9 mmHg and 6.0 vs 5.6 mmol/l, respectively). The relationship in females was non-significant. The age-adjusted odds ratios (OR [95% CI]) of having elevated low density lipoprotein cholesterol, total cholesterol, glucose and blood pressure in male HAB vs male NHAB were 0.61 [0.32. 1.16], 0.64 [0.33, 1.23], 1.52 [0.80, 2.88] and 2.11 [0.88, 5.23], and in female HAB vs female NHAB - 0.59 [0.31, 1.12], 0.64 [0.32, 1.26], 0.87 [0.40, 1.79] and 1.86 [0.70, 4.68], respectively. CONCLUSIONS: Adequately planned occupational medicine examinations provide an opportunity to diagnose dyslipidaemia, hyperglycaemia, or high BP in all groups of employees, including highly educated academics.

[5] *Kelsey M, Page C, Alhanti B et al.* **Lipoprotein(a) Testing Patterns in a Large Health System**. The American journal of cardiology 2021; 153:43-50.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34210501
ABSTRACT
Lipoprotein (a) [Lp(a)] is associated with increased risk of atherosclerotic cardiovascular disease (ASCVD). As directed therapy for Lp(a) emerges, it is important to understand patterns of Lp(a) testing in routine clinical practice. We set out to characterize Lp(a) testing across a large academic health system. Using electronic health record (EHR) data from 2014 to 2019, we compared patients who underwent Lp(a) testing to date-matched peers who had low density lipoprotein (LDL-C) assessment alone. We analyzed ordering provider characteristics and rates of initiation of new lipid

lowering therapy (LLT) within 12 months after testing. Of 1,296 adults with Lp(a) test results, 629 (48.5%) had prior history of ASCVD and 667 (51.4%) did not. Compared with those with LDL-C testing alone, individuals who underwent Lp(a) testing were more like to have a myocardial infarction or ischemic stroke at a young age and multiple prior cardiovascular events. Though the majority of Lp(a) tests were ordered in outpatient encounters, a higher proportion of Lp(a) tests compared with LDL-C tests were performed in the inpatient setting. Neurology and psychiatry were the most common specialty to order Lp(a) tests in our cohort. There was a significantly increased initiation of LLT after Lp(a) testing compared with LDL-C testing across all medication types. Consistent with guidelines, Lp(a) testing is used in those with early onset ASCVD, and among those with multiple cardiovascular events. Lp(a) testing is associated with more aggressive LLT in following year. Further research is needed to characterize Lp(a) testing across larger populations.

[6] *Beydoun MA, Weiss J, Beydoun HA et al.* **Race, APOE genotypes, and cognitive decline among middle-aged urban adults**. Alzheimer's research & therapy 2021; 13:120.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34193248
ABSTRACT
BACKGROUND: Associations of Apolipoprotein (APOE) ε2 or ε4 (APOE2 or APOE4) dosages with cognitive change may differ across racial groups. METHODS: Longitudinal data on 1770 middle-aged White and African American adults was compiled from the Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS 2004-2013) study. APOE2 and APOE4 dosages were the two main exposures, while v(1) and annual rate of change in cognitive performance (between v(1) and v(2)) on 11 test scores were the main outcomes of interest (v1: 2004-2009 and v2: 2009-2013). Mixed-effects linear regression models were conducted adjusting for socio-demographic, lifestyle, and health-related potential confounders. Race (African American vs. White) and sex within racial groups were main effect modifiers. RESULTS: Upon adjustment for multiple testing and potential confounders, APOE4 allelic dosage was associated with faster decline on a test of verbal memory among Whites only (CVLT-List A: $\gamma(12) = -0.363 \pm 0.137$, $p = 0.008$), but not among African Americans. In contrast, among African American women, APOE4 dosage was linked to slower decline on a test of attention (BTA: $\gamma(12) = +0.106 \pm 0.035$, $p = 0.002$), while no association was detected among African American men. APOE2 and APOE4 dosages showed inconsistent results in other domains of cognition overall and across racial groups that did not survive correction for multiple testing. CONCLUSIONS: In conclusion, APOE4 dosage was associated with faster decline on a test of verbal memory among Whites only, while exhibiting a potential protective effect among African American women in the domain of attention. Further longitudinal studies are needed to replicate our race and sex-specific findings.

[7] *Bangen KJ, Smirnov DS, Delano-Wood L et al.* **Arterial stiffening acts synergistically with APOE genotype and AD biomarker status to influence memory in older adults without dementia**. Alzheimer's research & therapy 2021; 13:121.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34210365
ABSTRACT
BACKGROUND: Arterial stiffening has emerged as an important risk factor for Alzheimer's disease (AD) and related dementias. Carotid-femoral pulse wave velocity has been proposed as a non-invasive and reproducible method to assess arterial stiffness. However, the association of pulse wave

velocity with performance across multiple cognitive domains as well as interactions with in vivo AD biomarkers and apolipoprotein E (APOE) genotype has received limited study. METHOD: We studied 193 older adult volunteers (167 with normal cognition and 26 with mild cognitive impairment) who underwent comprehensive medical and neuropsychological evaluation at the University of California, San Diego Alzheimer's Disease Research Center. Cerebrospinal fluid (CSF) biomarkers were available on 123 participants (63%). Linear models examined whether pulse wave velocity significantly interacted with APOE ε4 status and CSF AD biomarker positivity (based on the ratio of total tau over beta-amyloid [tau/Aβ(42)]) on memory, language, executive functioning, attention, and visuospatial abilities. RESULTS: After adjusting for demographic characteristics and vascular risk burden, across the entire sample, pulse wave velocity was associated with poorer executive functioning but not the performance in the other cognitive domains. When the modifying effects of AD genetic risk and CSF AD biomarkers were considered, pulse wave velocity interacted with APOE genotype and CSF tau/Aβ ratio such that a stronger association between elevated pulse wave velocity and poorer memory performance was found among those positive for CSF and genetic AD markers. There were no significant interaction effects for non-memory cognitive domains. CONCLUSION: The findings suggest that pulse wave velocity, a non-invasive method to assess arterial wall properties, may be a useful marker of risk for cognitive decline, particularly among individuals who are APOE ε4 carriers or CSF AD biomarke0r-positive.

[8] *van Dam-Nolen DHK, van Dijk AC, Crombag G et al.* **Lipoprotein(a) levels and atherosclerotic plaque characteristics in the carotid artery: The Plaque at RISK (PARISK) study**. Atherosclerosis 2021; 329:22-29.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34216874

ABSTRACT

BACKGROUND AND AIMS: Lipoprotein(a) is an independent risk factor for cardiovascular disease and recurrent ischemic stroke. Lipoprotein(a) levels are known to be associated with carotid artery stenosis, but the relation of lipoprotein(a) levels to carotid atherosclerotic plaque composition and morphology is less known. We hypothesize that higher lipoprotein(a) levels and lipoprotein(a)-related SNPs are associated with a more vulnerable carotid plaque and that this effect is sex-specific. METHODS: In 182 patients of the Plaque At RISK study we determined lipoprotein(a) concentrations, apo(a) KIV-2 repeats and LPA SNPs. Imaging characteristics of carotid atherosclerosis were determined by MDCTA (n = 161) and/or MRI (n = 171). Regressions analyses were used to investigate sex-stratified associations between lipoprotein(a) levels, apo(a) KIV-2 repeats, and LPA SNPs and imaging characteristics. RESULTS: Lipoprotein(a) was associated with presence of lipid-rich necrotic core (LRNC) (aOR = 1.07, 95% CI: 1.00; 1.15), thin-or-ruptured fibrous cap (TRFC) (aOR = 1.07, 95% CI: 1.01; 1.14), and degree of stenosis (β = 0.44, 95% CI: 0.00; 0.88). In women, lipoprotein(a) was associated with presence of intraplaque hemorrhage (IPH) (aOR = 1.25, 95% CI: 1.06; 1.61). In men, lipoprotein(a) was associated with degree of stenosis (β = 0.58, 95% CI: 0.04; 1.12). Rs10455872 was significantly associated with increased calcification volume (β = 1.07, 95% CI: 0.25; 1.89) and absence of plaque ulceration (aOR = 0.25, 95% CI: 0.04; 0.93). T3888P was associated with absence of LRNC (aOR = 0.36, 95% CI: 0.16; 0.78) and smaller maximum vessel wall area (β = -10.24, 95%CI: -19.03; -1.44). CONCLUSIONS: In patients with symptomatic carotid artery stenosis, increased lipoprotein(a) levels were associated with degree of stenosis, and IPH, LRNC, and TRFC, known as vulnerable plaque characteristics, in the carotid artery. T3888P was

associated with lower LRNC prevalence and smaller maximum vessel wall area. Further research in larger study populations is needed to confirm these results.

[9] *Teymoori F, Farhadnejad H, Mokhtari E et al.* **Dietary and lifestyle inflammatory scores and risk of incident diabetes: a prospective cohort among participants of Tehran lipid and glucose study**. BMC public health 2021; 21:1293.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34215245
ABSTRACT
BACKGROUND: Inflammation is a precursor of chronic disease, which is affected by lifestyle and dietary habits. Recently empirical dietary inflammatory patterns (EDIP), dietary inflammation scores (DIS), and lifestyle inflammation scores (LIS) were developed to indicate lifestyle and dietary contributions in systemic inflammation. The current study aimed to investigate the associations between these indices and the incidence of diabetes among Tehranian adults. METHODS: A total of 4624 individuals, aged 20-75 years, who were free of diabetes at baseline (2008-2011), were followed for 5.71 years (2014-2017) to ascertain incident diabetes. Dietary intakes were collected at baseline using the food frequency questionnaire. The hazard ratio (HR) of diabetes was calculated by Cox proportional hazards regression across quartiles of EDIP, DIS, and LIS, adjusted for potential confounders. RESULTS: The mean ± SD for the age and BMI of the study population (45.1% male) were 40.8 ± 12.7 years and 27.1 ± 4.1 Kg.m2, respectively. At the end of the follow-up, 329 (7.1%) diabetes cases were identified. In the multivariable-adjusted model, individuals in the highest compared to the lowest quartile of EDIP (HR = 0.83; 95%CI:0.59-1.15, p for trend = 0.286), and LIS (HR = 2.41; 95%CI:1.61-3.60, P for trend < 0.001) had increased risk of diabetes. However, no significant associations were found between the score of DIS and diabetes incidents (HR = 0.83; 95%CI:0.59-1.15, p for trend = 0.286). CONCLUSION: Greater adherence to EDIP and LIS scores was associated with a higher risk of diabetes, while no significant association was found between the DIS score and diabetes incident.

[10] *Ponte-Negretti CI, Wyss FS, Piskorz D et al.* **Latin American Consensus on management of residual cardiometabolic risk. A consensus paper prepared by the Latin American Academy for the Study of Lipids and Cardiometabolic Risk (ALALIP) endorsed by the Inter-American Society of Cardiology (IASC), the International Atherosclerosis Society (IAS), and the Pan-American College of Endothelium (PACE)**. Archivos de cardiologia de Mexico 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34187049
ABSTRACT
BACKGROUND: Hypertension, hyperglycemia, dyslipidemia, overweight, obesity, and tobacco (smoking, chewing, and vaping), together with a pro-inflammatory and procoagulant state, are the main risk factors related to atherosclerotic cardiovascular disease. OBJECTIVE AND METHODS: A group of experts from the Americas, based on their clinical expertise in cardiology, cardiovascular prevention, and cardiometabolic (CM) diseases, joined together to develop these practical recommendations for the optimal evaluation and treatment of residual CM risk factors in Latin America, using a modified Delphi methodology (details in electronic TSI) to generate a comprehensive CM risk reduction guideline, and through personalized medicine and patient-centered decision, considering the cost-benefit ratio The process was well defined to avoid conflicts of interest that could bias the discussion and recommendations. RESULTS: Residual risk reduction should

consider therapeutic options adapted to specific patient needs, based on five treatment objectives: triglyceride-rich lipoproteins, inflammation, impaired glucose metabolism, high blood pressure, and prothrombotic status. Comprehensive control of all CM risk factors should be a priority to deal with this important public health problem and prevent premature deaths. The recommendations in this paper address the evidence-based treatment of CM risk and are intended for clinical application in Latin American countries.

[11] *McNamara RK, Li W, Lei D et al.* **Fish oil supplementation alters emotion-generated corticolimbic functional connectivity in depressed adolescents at high-risk for bipolar I disorder: A 12-week placebo-controlled fMRI trial**. Bipolar Disord 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34214231

ABSTRACT

OBJECTIVE: To evaluate the effects of fish oil (FO), a source of the omega-3 polyunsaturated fatty acids (n-3 PUFA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), on emotion-generated corticolimbic functional connectivity in depressed youth at high risk for developing bipolar I disorder. METHODS: Thirty-nine antidepressant-free youth with a current depressive disorder diagnosis and a biological parent with bipolar I disorder were randomized to 12-week double-blind treatment with FO or placebo. At baseline and endpoint, fMRI (4 Tesla) scans were obtained while performing a continuous performance task with emotional and neutral distractors (CPT-END). Seed-to-voxel functional connectivity analyses were performed using bilateral orbitofrontal cortex (OFC) and amygdala (AMY) seeds. Measures of depression, mania, global symptom severity, and erythrocyte fatty acids were obtained. RESULTS: Erythrocyte EPA+DHA composition increased significantly in the FO group (+47%, $p \leq 0.0001$) but not in the placebo group (-10%, $p = 0.11$). Significant group by time interactions were found for functional connectivity between the left OFC and the left superior temporal gyrus (STG) and between the right AMY and right inferior temporal gyrus (ITG). OFC-STG connectivity increased in the FO group ($p = 0.0001$) and decreased in the placebo group ($p = 0.0019$), and AMY-ITG connectivity decreased in the FO group ($p = 0.0014$) and increased in the placebo group ($p < 0.0001$). In the FO group, but not placebo group, the decrease in AMY-ITG functional connectivity correlated with decreases in Childhood Depression Rating Scale-Revised and Clinical Global Impression-Severity Scale scores. CONCLUSIONS: In depressed high-risk youth FO supplementation alters emotion-generated corticolimbic functional connectivity which correlates with changes in symptom severity ratings.

[12] *Mayo J, Hoffman T, Smith R, Kellicut D*. **Lipoprotein(a) as a unique primary risk factor for early atherosclerotic peripheral arterial disease**. BMJ case reports 2021; 14.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34193454

ABSTRACT

Elevated plasma lipoprotein(a) is a relatively common condition that contributes to many cardiovascular diseases. However, the awareness and testing for this condition remain low. Herein, we present a case of an otherwise healthy and active man who developed symptoms of peripheral arterial disease starting at age 49, and was found to have hyper-lipoprotein(a) as his only notable risk factor. Diagnosis was not made until years later, after an extensive workup. Upon further screening, he was also found to have subclinical coronary and carotid artery atherosclerotic disease. The patient was treated with aspirin, statin, niacin and angioplasty to bilateral superficial femoral arteries with

good symptom resolution. Early screening of his son also revealed a similarly elevated lipoprotein(a) level. It is important to raise awareness of this condition and its relationship to early-onset peripheral arterial disease so patients and their families can be appropriately identified, counselled and treated.

[13] *Malo AI, Girona J, Ibarretxe D et al.* **Serum glycoproteins A and B assessed by (1)H-NMR in familial hypercholesterolemia**. Atherosclerosis 2021; 330:1-7.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34218212
ABSTRACT
BACKGROUND AND AIMS: Inflammation is a pathophysiological mechanism of atherosclerosis, and several mediators have been proposed as biomarkers. Acute-phase serum glycoproteins are upregulated in the liver during systemic inflammation. Because of their unique biochemical characteristics, they can be measured by (1)H-NMR, and their role as subclinical inflammation markers is under clinical evaluation. We aimed to assess the clinical value of plasma glycoproteins in familial hypercholesterolemia (FH) patients. METHODS: We recruited 295 FH patients (75.6% with FH-associated genetic variants). At baseline, a full glycoprotein profile, glycoprotein A and B (GlycA and B) concentrations and their height and width ratios (H/W) were analysed by (1)H-NMR. A carotid artery ultrasound study was performed at baseline and prospectively at the 5-year follow-up in 144 FH patients. RESULTS: At baseline, the GlycA and GlycB concentrations and their H/W ratios were correlated with lipid profile and adiposity parameters, with the correlation between the GlycA and triglyceride concentrations ($r = 0.780$; $p < 0001$) being the strongest. Glycoprotein concentrations were also correlated with inflammation markers, mainly hsCRP. Higher glycoprotein concentrations were observed in patients with higher intima media thickness, arterial rigidity and presence of arteriosclerotic plaques. In the multivariate and random forest analyses, the baseline GlycB concentration showed a significant contribution to the detection of FH individuals prone to develop carotid plaques. CONCLUSIONS: The concentrations of serum glycoproteins as assessed by (1)H-NMR are robust markers of subclinical inflammation. In FH patients, they are increased in the presence of subclinical vascular damage and could be considered atherosclerosis risk markers in the long term.

[14] *Kumric M, Borovac JA, Martinovic D et al.* **Circulating Biomarkers Reflecting Destabilization Mechanisms of Coronary Artery Plaques: Are We Looking for the Impossible?** Biomolecules 2021; 11.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34198543
ABSTRACT
Despite significant strides to mitigate the complications of acute coronary syndrome (ACS), this clinical entity still represents a major global health burden. It has so far been well-established that most of the plaques leading to ACS are not a result of gradual narrowing of the vessel lumen, but rather a result of sudden disruption of vulnerable atherosclerotic plaques. As most of the developed imaging modalities for vulnerable plaque detection are invasive, multiple biomarkers were proposed to identify their presence. Owing to the pivotal role of lipids and inflammation in the pathophysiology of atherosclerosis, most of the biomarkers originated from one of those processes, whereas recent advancements in molecular sciences shed light on the use of microRNAs. Yet, at present there are no clinically implemented biomarkers or any other method for that matter that could non-invasively, yet reliably, diagnose the vulnerable plaque. Hence, in this review we summarized the available

knowledge regarding the pathophysiology of plaque instability, the current evidence on potential biomarkers associated with plaque destabilization and finally, we discussed if search for biomarkers could one day bring us to non-invasive, cost-effective, yet valid way of diagnosing the vulnerable, rupture-prone coronary artery plaques.

[15] *Gutierrez-Mariscal FM, de la Cruz-Ares S, Torres-Peña JD et al.* **Coenzyme Q(10) and Cardiovascular Diseases**. Antioxidants (Basel, Switzerland) 2021; 10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34205085
ABSTRACT
Coenzyme Q(10) (CoQ(10)), which plays a key role in the electron transport chain by providing an adequate, efficient supply of energy, has another relevant function as an antioxidant, acting in mitochondria, other cell compartments, and plasma lipoproteins. CoQ(10) deficiency is present in chronic and age-related diseases. In particular, in cardiovascular diseases (CVDs), there is a reduced bioavailability of CoQ(10) since statins, one of the most common lipid-lowering drugs, inhibit the common pathway shared by CoQ(10) endogenous biosynthesis and cholesterol biosynthesis. Different clinical trials have analyzed the effect of CoQ(10) supplementation as a treatment to ameliorate these deficiencies in the context of CVDs. In this review, we focus on recent advances in CoQ(10) supplementation and the clinical implications in the reduction of cardiovascular risk factors (such as lipid and lipoprotein levels, blood pressure, or endothelial function) as well as in a therapeutic approach for the reduction of the clinical complications of CVD.

[16] *Božina N, Ganoci L, Simičević L et al.* **Drug-drug-gene interactions as mediators of adverse drug reactions to diclofenac and statins: a case report and literature review**. Arhiv za higijenu rada i toksikologiju 2021; 72:114-128.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34187111
ABSTRACT
Concomitant treatment with drugs that inhibit drug metabolising enzymes and/or transporters, such as commonly prescribed statins and nonsteroidal anti-inflammatory drugs (NSAIDs), has been associated with prolonged drug exposure and increased risk of adverse drug reactions (ADRs) due to drug-drug interactions. The risk is further increased in patients with chronic diseases/comorbidities who are more susceptible because of their genetic setup or external factors. In that light, we present a case of a 46-year-old woman who had been experiencing acute renal and hepatic injury and myalgia over two years of concomitant treatment with diclofenac, atorvastatin, simvastatin/fenofibrate, and several other drugs, including pantoprazole and furosemide. Our pharmacogenomic findings supported the suspicion that ADRs, most notably the multi-organ toxicity experienced by our patient, may be owed to drug-drug-gene interactions and increased bioavailability of the prescribed drugs due to slower detoxification capacity and decreased hepatic and renal elimination. We also discuss the importance of CYP polymorphisms in the biotransformation of endogenous substrates such as arachidonic acid and their modulating role in pathophysiological processes. Yet even though the risks of ADRs related to the above mentioned drugs are substantially evidenced in literature, pre-emptive pharmacogenetic analysis has not yet found its way into common clinical practice.

[17] *Ali AA, Fasen M, Ng K, Shelley P*. **Lipaemic blood: alcohol-induced acute hypertriglyceridaemia**. BMJ case reports 2021; 14.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34210703
ABSTRACT

[18] *Zapatero-Belinchón FJ, Ötjengerdes R, Sheldon J et al.* **Interdependent Impact of Lipoprotein Receptors and Lipid-Lowering Drugs on HCV Infectivity**. Cells 2021; 10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34209751
ABSTRACT
The HCV replication cycle is tightly associated with host lipid metabolism: Lipoprotein receptors SR-B1 and LDLr promote entry of HCV, replication is associated with the formation of lipid-rich membranous organelles and infectious particle assembly highjacks the very-low-density lipoprotein (VLDL) secretory pathway. Hence, medications that interfere with the lipid metabolism of the cell, such as statins, may affect HCV infection. Here, we study the interplay between lipoprotein receptors, lipid homeostasis, and HCV infection by genetic and pharmacological interventions. We found that individual ablation of the lipoprotein receptors SR-B1 and LDLr did not drastically affect HCV entry, replication, or infection, but double lipoprotein receptor knock-outs significantly reduced HCV infection. Furthermore, we could show that this effect was neither due to altered expression of additional HCV entry factors nor caused by changes in cellular cholesterol content. Strikingly, whereas lipid-lowering drugs such as simvastatin or fenofibrate did not affect HCV entry or infection of immortalized hepatoma cells expressing SR-B1 and/or LDLr or primary human hepatocytes, ablation of these receptors rendered cells more susceptible to these drugs. Finally, we observed no significant differences between statin users and control groups with regards to HCV viral load in a cohort of HCV infected patients before and during HCV antiviral treatment. Interestingly, statin treatment, which blocks the mevalonate pathway leading to decreased cholesterol levels, was associated with mild but appreciable lower levels of liver damage markers before HCV therapy. Overall, our findings confirm the role of lipid homeostasis in HCV infection and highlight the importance of the mevalonate pathway in the HCV replication cycle.

[19] *Vargas-Alarcón G, Pérez-Méndez O, González-Pacheco H et al.* **The rs508487, rs236911, and rs236918 Genetic Variants of the Proprotein Convertase Subtilisin-Kexin Type 7 (PCSK7) Gene Are Associated with Acute Coronary Syndrome and with Plasma Concentrations of HDL-Cholesterol and Triglycerides**. Cells 2021; 10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34207761
ABSTRACT
Dyslipidemia has a substantial role in the development of acute coronary syndrome (ACS). Previous reports, including genome-wide associations studies (GWAS), have shown that some genetic variants of the proprotein convertase subtilisin-kexin type 7 (PCSK7) gene are associated with plasma lipid levels. In the present study, we evaluated whether PCSK7 gene polymorphisms are significantly associated with the plasma lipid profile and ACS. Three PCSK7 gene polymorphisms (rs508487 T/C, rs236911 C/A, and rs236918 C/G) were determined using TaqMan genotyping assays in a group of 603 ACS patients and 622 healthy controls. The plasma lipid profile was determined in the study groups by enzymatic/colorimetric assays. Under the recessive model, the rs236918 C allele was associated with a high risk of ACS (OR = 2.11, pC = 0.039). In the same way, under the recessive and additive models, the rs236911 C allele was associated with a high risk of ACS (OR = 1.95, pC = 0.037, and OR = 1.28, pC = 0.037, respectively). In addition, under the co-dominant model, the

rs508487 T allele was associated with a higher risk of ACS (OR = 1.78, pC = 0.010). The CCC and TCC haplotypes were associated with a high risk of ACS (OR = 1.21, pC = 0.047, and OR = 1.80, pC = 0.001, respectively). The rs236911 CC and rs236918 CC genotypes were associated with lower high-density lipoproteins-cholesterol (HDL-C) plasma concentrations, whereas the rs236911 CC genotype was associated with a higher concentration of triglycerides, as demonstrated in the control individuals who were not receiving antidyslipidemic drugs. Our data suggest that the PCSK7 rs508487 T/C, rs236911 C/A, and rs236918 C/G polymorphisms are associated with the risk of developing ACS, and with plasma concentrations of HDL-C and triglycerides.

[20] *Su X, Chen X, Wang B*. **Pathology of metabolically-related dyslipidemia**. Clinica chimica acta; international journal of clinical chemistry 2021; 521:107-115.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34192528
ABSTRACT
It is well established that overweight/obesity is closely associated with multiple health problems. Among these, dyslipidemia is the most important and main driving force behind pathologic development of cardio-metabolic disorders such as diabetes mellitus, atherosclerotic-related cardiovascular disease and hypertension. Notably, a subtype of dyslipidemia, metabolic related dyslipidemia, is now recognized as a vital link between obesity and multiple different cardiovascular diseases. This condition is characterized by increased low density lipoprotein cholesterol (LDL-C) and triglyceride (TG) and very low density lipoprotein cholesterol (VLDL-C) as well as decreased high density lipoprotein cholesterol (HDL-C) in serum. In this review, we summarize the current understanding of metabolic related dyslipidemia and the potential mechanisms which lead to the pathogenesis of obesity/overweight. We focus on several novel lipid biomarkers such as pro-protein convertase subtilisin/kexin type 9 (PCSK9) and sphingosine-1-phosphate (S1P) and their potential use as biomarkers of metabolic related dyslipidemia.

[21] *Nicholls SJ, Bubb KJ*. **The Riskier Lipid: What Is on the HORIZON for Lipoprotein (a) and Should There Be Lp(a) Screening for All?** Current cardiology reports 2021; 23:97.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34196823
ABSTRACT
PURPOSE OF REVIEW: Despite widespread targeting of cardiovascular risk factors, many patients continue to experience clinical events. This residual risk has stimulated efforts to develop novel therapeutic approaches to target additional factors underscoring cardiovascular disease. This review aimed to summarize existing evidence supporting targeting of Lp(a) as a novel cardioprotective strategy. RECENT FINDINGS: Increasing evidence has implicated lipoprotein (a) [Lp(a)] in the pathogenesis of both atherosclerotic and calcific aortic valve disease. Therapeutic advances have produced novel agents that selectively lower Lp(a) levels, which have now progressed to evaluate their impact on cardiovascular events in large clinical outcome trials. Evidence continues to accumulate suggesting that targeting Lp(a) may be effective in reducing cardiovascular risk. With advances in Lp(a) targeted therapeutics, clinical trials now have the opportunity to determine whether this strategy will be effective for high-risk patients.

[22] *Muse ED, Chen SF, Torkamani A*. **Monogenic and Polygenic Models of Coronary Artery Disease**. Current cardiology reports 2021; 23:107.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34196841

ABSTRACT

PURPOSE OF THE REVIEW: Coronary artery disease (CAD) is a common disease globally attributable to the interplay of complex genetic and lifestyle factors. Here, we review how genomic sequencing advances have broadened the fundamental understanding of the monogenic and polygenic contributions to CAD and how these insights can be utilized, in part by creating polygenic risk estimates, for improved disease risk stratification at the individual patient level. RECENT FINDINGS: Initial studies linking premature CAD with rare familial cases of elevated blood lipids highlighted high-risk monogenic contributions, predominantly presenting as familial hypercholesterolemia (FH). More commonly CAD genetic risk is a function of multiple, higher frequency variants each imparting lower magnitude of risk, which can be combined to form polygenic risk scores (PRS) conveying significant risk to individuals at the extremes. However, gaps remain in clinical validation of PRSs, most notably in non-European populations. With improved and more broadly utilized genomic sequencing technologies, the genetic underpinnings of coronary artery disease are being unraveled. As a result, polygenic risk estimation is poised to become a widely used and powerful tool in the clinical setting. While the use of PRSs to augment current clinical risk stratification for optimization of cardiovascular disease risk by lifestyle change or therapeutic targeting is promising, we await adequately powered, prospective studies, demonstrating the clinical utility of polygenic risk estimation in practice.

[23] *Mesi O, Lin C, Ahmed H, Cho LS*. **Statin intolerance and new lipid-lowering treatments**. Cleveland Clinic journal of medicine 2021; 88:381-387.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34210712

ABSTRACT

[24] *Jin J, Shi Z, Pang X*. **Association between low-density lipoprotein cholesterol level and mortality in patients with cardiogenic shock: a retrospective cohort study**. BMJ open 2021; 11:e044668.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34215599

ABSTRACT

AIMS: Inflammation plays a key role in the pathophysiology of cardiogenic shock (CS). Low-density lipoprotein cholesterol (LDL-C) is a biomarker of inflammation and is used to predict prognostic outcomes of several diseases. The primary purpose of this study was to evaluate if LDL-C can be used as a biomarker to predict the mortality of CS. METHODS AND RESULTS: Records of critically ill patients with CS were identified from the Medical Information Mart for Intensive Care III database. A multivariate Cox regression model was employed to adjust for imbalances by incorporating parameters and potential confounders.A total of 551 critically ill patients with CS were enrolled for this analysis, including 207 with LDL-C <1.8 mmol/L and 344 with LDL-C ≥1.8 mmol/L. Results of multivariate Cox regression models found that higher concentration of LDL-C (LDL-C ≥1.8mmol/L) was associated with a reduced risk of in-hospital mortality (HR 0.66, 95% CI 0.50 to 0.87; p=0.003) and 28-day mortality (HR 0.61, 95% CI 0.46 to 0.80; p=0.002) LDL-C in patients with CS. Patients with LDL-C ≥1.8 mmol/L were independently associated with improved in-hospital survival (HR 0.32, 95% CI 0.20 to 0.52, p<0.001) and 28-day survival (HR 0.51, 95% CI 0.33 to 0.73, p=0.002) compared with patients with LDL-C <1.8 mmol/L. The impact of LDL-C on in-hospital mortality and 28-day

mortality persisted in patients with acute coronary syndrome (ACS) and was not statistically significant in the non-ACS subgroup. CONCLUSIONS: Our study observed that increased LDL-C level was related with improved survival in patients with CS, but not with improved outcomes in patients with uncomplicated ACS. The results need to be verified in randomised controlled trials.

[25] *Hanson CA, Lu E, Ghumman SS et al.* **Long-term outcomes in patients with normal coronary arteries, nonobstructive, or obstructive coronary artery disease on invasive coronary angiography**. Clinical cardiology 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34216037
ABSTRACT
BACKGROUND: Normal or near normal coronary arteries (NNCA) or nonobstructive coronary artery disease (CAD) are commonly found on invasive coronary angiography (ICA). HYPOTHESIS: We aimed to determine long-term outcomes by severity of CAD in a contemporary cohort of patients undergoing ICA for evaluation for ischemic heart disease. METHODS: We assessed a consecutive cohort of 925 patients who underwent non-emergent ICA over 24 months. Cardiac death (CD), nonfatal myocardial infarction (NFMI), late revascularization, and medication use were assessed. RESULTS: Follow-up data was available in 850 patients. Of patients without heart failure, at a median of 6.0 years, there was a significant decrease in survival free from CD or NFMI, and from all cardiac events, for those with obstructive CAD compared with patients with NNCAs or nonobstructive CAD ($p < .001$ for both). No differences between NNCA and nonobstructive CAD patients in rates of CD or NFMI (2.0% vs. 2.1%/year, $p = .58$) or all cardiac events (2.4% vs. 2.9%/year, $p = .84$) were observed. CONCLUSION: Long-term follow-up in a contemporary cohort of consecutive patients undergoing non-emergent ICA for detection of CAD showed no difference in annual rates of CD or NFMI, or total cardiac events, in patients with NNCAs versus those with nonobstructive CAD, whereas patients with obstructive CAD had significantly more events. Event rates were low and similar by gender. Use of aspirin, lipid lowering therapy, and beta-blockers increased in all subgroups after ICA. We speculate this may explain the low incidence of subsequent cardiac events, and similar event rates in patients with NNCA and nonobstructive CAD, even in patients presenting with non-ST-elevation MI.

[26] *Ghernautan V, Amini M, Sachmechi I*. **Maculopapular Exanthema After the Second Dose of Evolocumab**. Cureus 2021; 13:e15249.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34188988
ABSTRACT
Evolocumab is a relatively new monoclonal antibody designed to decrease low-density lipoproteins via the inhibition of proprotein convertase subtilisin/kexin type 9 (PCSK9). It is used alone or in combination with other lipid-lowering agents. Evolocumab was associated with adverse events of skin rashes in clinical trials. We describe a rare case of maculopapular exanthema in a female patient with hyperlipidemia, which was treated with evolocumab. The patient was a 60-year-old female with hyperlipidemia who experienced a maculopapular rash after she was administered the second dose of evolocumab subcutaneously. The rash occurred on her torso and upper extremities and was associated with pruritus and mild wheezing. The hypersensitivity reaction was treated with antihistamines and with the discontinuation of evolocumab. The skin eruption cleared within 10 days.

In conclusion, medical professionals should be aware of evolocumab skin hypersensitivity reactions, which could demand the cessation of the evolocumab treatment.

[27] *Cabré N, Duan Y, Llorente C et al.* **Colesevelam Reduces Ethanol-Induced Liver Steatosis in Humanized Gnotobiotic Mice**. Cells 2021; 10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34198609
ABSTRACT
Alcohol-related liver disease is associated with intestinal dysbiosis. Functional changes in the microbiota affect bile acid metabolism and result in elevated serum bile acids in patients with alcohol-related liver disease. The aim of this study was to identify the potential role of the bile acid sequestrant colesevelam in a humanized mouse model of ethanol-induced liver disease. We colonized germ-free (GF) C57BL/6 mice with feces from patients with alcoholic hepatitis and subjected humanized mice to the chronic-binge ethanol feeding model. Ethanol-fed gnotobiotic mice treated with colesevelam showed reduced hepatic levels of triglycerides and cholesterol, but liver injury and inflammation were not decreased as compared with non-treated mice. Colesevelam reduced hepatic cytochrome P450, family 7, subfamily a, polypeptide 1 (Cyp7a1) protein expression, although serum bile acids were not lowered. In conclusion, our findings indicate that colesevelam treatment mitigates ethanol-induced liver steatosis in mice.

[28] *Sheehan OC, Dhamoon MS, Bettger JP et al.* **Racial differences in persistence to secondary prevention medication regimens after ischemic stroke**. Ethn Health 2021:1-13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34196573
ABSTRACT
BACKGROUND: Prior stroke is one of the biggest risk factors for future stroke events. Effective secondary prevention medication regimens can dramatically reduce recurrent stroke risk. Guidelines recommend the use of antithrombotic, antihypertensive and lipid-lowering medications after stroke. Medication adherence is known to be better in the presence of a caregiver but long-term adherence after stroke is unknown and disparities may persist. METHODS: We examined the effects of race and sex on baseline prescription and maintenance of secondary prevention regimens in the presence of a caregiver using the Caring for Adults Recovering from the Effects of Stroke (CARES) study, an ancillary study of the national REasons for Geographic and Racial Differences in Stroke (REGARDS). RESULTS: Incident ischemic stroke survivors (N = 172; 36% Black) with family caregivers had medications recorded at hospital discharge and on average 9.8 months later during a home visit. At discharge, antithrombotic prescription (95.9%), lipid-lowering medications (78.8%) and antihypertensives (89.9%) were common and there were no race or sex differences in discharge prescription rates. One year later, medication persistence had fallen to 86.6% for antithrombotics ($p = 0.002$) and 69.8% for lipid lowering ($p = 0.008$) but increased to 93.0% for antihypertensives ($p = 0.30$). Blacks were more likely to have discontinued antithrombotics than Whites (18.3% v 7.7%, $p = 0.04$). No significant differences in persistence were seen with age, sex, income, depression, or cognitive impairment. CONCLUSIONS: Medication persistence was high in this sample, likely due to the presence of a caregiver. In our cohort, despite similar prescription rates at the time of hospital discharge, Black stroke survivors were more than twice as likely to stop antithrombotics than Whites. The effect of changes in patterns of medication usage on health outcomes in Black stroke survivors warrants continued investigation.

[29] *Ruscica M, Macchi C, Iodice S et al.* **Prognostic parameters of in-hospital mortality in COVID-19 patients-An Italian experience**. European journal of clinical investigation 2021; 51:e13629.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34184268
ABSTRACT
Background During COVID-19 outbreak, Italy was the first country in Europe to be heavily affected with an intensive care unit mortality of 26%. In order to reduce this percentage, physicians should establish clear and objective criteria to stratify COVID-19 patients at high risk of in-hospital death. Thus, the aim has been to test a large spectrum of variables ranging from clinical evaluation to laboratory biomarkers to identify which parameter would best predict all-cause in-hospital mortality in COVID-19 patients. Design observational study. Results Multivariate Cox regression analysis showed that each 5 years of increase in age corresponded to a hazard ratio (HR) of 1.28 (95% CI 1.00-1.65, P = .050); each increment of 803 ng/L of N-terminal pro-B-type natriuretic peptide (NT-proBNP) corresponded to a HR of 1.24 (95% CI 1.11-1.39, P < .001); each increment of 58 ng/L of interleukin (IL)-6 corresponded to a HR of 1.23 (95% CI 1.09-1.40, P < .001), and each increment of 250 U/L of lactate dehydrogenase (LDH) corresponded to a HR of 1.23 (95% CI 1.10-1.37, P < .001). According to the calculated cut-points for age (≥70 years), NT-proBNP (≥803 ng/L), IL-6 (≥58 ng/L) and LDH (≥371 U/L) when 2 out of these 4 were overcome, the HR was 2.96 (95% CI 1.97-4.45, P < .001). Conclusion In COVID-19 patients, besides age, the evaluation of three biochemical parameters, available in few hours after hospital admission can predict in-hospital mortality regardless of other comorbidities.

[30] *Retnakaran R, Shah BR*. **Impact of pregnancy on the trajectories of cardiovascular risk factors in women with and without gestational diabetes**. Diabetes Obes Metab 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34189830
ABSTRACT
AIMS: The elevated lifetime risk of cardiovascular disease in women who develop gestational diabetes mellitus (GDM) has been attributed to adverse life-course trajectories of cardiovascular risk factors that arise before pregnancy and continue thereafter. We hypothesized that pregnancy may differentially affect these trajectories in women who develop GDM and those who do not. MATERIALS AND METHODS: With population-based administrative databases, we identified all nulliparous women in Ontario, Canada, who had singleton pregnancies between January 2011 and December 2016 and ≥2 measurements of the following analytes both before and after pregnancy: glycated haemoglobin (HbA1c), glucose, lipids and transaminases. In total, 39 581 women (4373 with GDM) had 3.9 ± 3.4 tests before and 4.6 ± 5.4 tests after pregnancy. RESULTS: Both before and after pregnancy, women who developed GDM had higher HbA1c, fasting glucose, low-density lipoprotein (LDL)-cholesterol and triglycerides than their peers, with lower high-density lipoprotein (HDL)-cholesterol (all p < .0001). Before pregnancy, women who went on to GDM had higher annual increases than their peers did in HbA1c, fasting glucose and triglycerides (all p ≤ .01); lesser annual decrease in LDL (p = .0003); and greater annual decrease in HDL (p = .0006). Compared with pre-pregnancy, the postpartum differences in annual rates of change in HbA1c and fasting glucose were 6.9- and 3.3-fold higher, respectively, in women with GDM. Conversely, the respective postpartum differences in annual rates of change in triglycerides, LDL and HDL were 1.2, 1.6 and 0.3 times lower

than before pregnancy. CONCLUSION: After pregnancy, differences in pregravid trajectories of glycaemic measures are amplified between women with GDM and their peers. In contrast, pregravid differences in lipid measures persist but do not differentially worsen after pregnancy.

[31] *Kronenberg F*. **Lipoprotein(a)**. Handbook of experimental pharmacology 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34196811

ABSTRACT

Lipoprotein(a) [Lp(a)] is an atherogenic lipoprotein with a strong genetic regulation. Up to 90% of the concentrations are explained by a single gene, the LPA gene. The concentrations show a several-hundred-fold interindividual variability ranging from less than 0.1 mg/dL to more than 300 mg/dL. Lp(a) plasma concentrations above 30 mg/dL and even more above 50 mg/dL are associated with an increased risk for cardiovascular disease including myocardial infarction, stroke, aortic valve stenosis, heart failure, peripheral arterial disease, and all-cause mortality. Since concentrations above 50 mg/dL are observed in roughly 20% of the Caucasian population and in an even higher frequency in African-American and Asian-Indian ethnicities, it can be assumed that Lp(a) is one of the most important genetically determined risk factors for cardiovascular disease.Carriers of genetic variants that are associated with high Lp(a) concentrations have a markedly increased risk for cardiovascular events. Studies that used these genetic variants as a genetic instrument to support a causal role for Lp(a) as a cardiovascular risk factor are called Mendelian randomization studies. The principle of this type of studies has been introduced and tested for the first time ever with Lp(a) and its genetic determinants.There are currently no approved pharmacologic therapies that specifically target Lp(a) concentrations. However, some therapies that target primarily LDL cholesterol have also an influence on Lp(a) concentrations. These are mainly PCSK9 inhibitors that lower LDL cholesterol by 60% and Lp(a) by 25-30%. Furthermore, lipoprotein apheresis lowers both, Lp(a) and LDL cholesterol, by about 60-70%. Some sophisticated study designs and statistical analyses provided support that lowering Lp(a) by these therapies also lowers cardiovascular events on top of the effect caused by lowering LDL cholesterol, although this was not the main target of the therapy. Currently, new therapies targeting RNA such as antisense oligonucleotides (ASO) or small interfering RNA (siRNA) against apolipoprotein(a), the main protein of the Lp(a) particle, are under examination and lower Lp(a) concentrations up to 90%. Since these therapies specifically lower Lp(a) concentrations without influencing other lipoproteins, they will serve the last piece of the puzzle whether a decrease of Lp(a) results also in a decrease of cardiovascular events.

[32] *Kotlęga D, Peda B, Palma J et al.* **Free Fatty Acids Are Associated with the Cognitive Functions in Stroke Survivors**. International journal of environmental research and public health 2021; 18.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34208689

ABSTRACT

Ischemic stroke is a leading cause of motor impairment and psychosocial disability. Although free fatty acids (FFA) have been proven to affect the risk of stroke and potentially dementia, the evidence of their impact on cognitive functions in stroke patients is lacking. We aimed to establish such potential relationships. Seventy-two ischemic stroke patients were prospectively analysed. Their cognitive functions were assessed seven days post-stroke and six months later as follow-up (n = 41). Seven days post-stroke analysis of serum FFAs levels showed direct correlations between Cognitive

Verbal Learning Test (CVLT) and the following FFAs: C20:4n6 arachidonic acid and C20:5n3 eicosapentaenoic acid, while negative correlations were observed for C18:3n3 linolenic acid (ALA), C18:4 n3 stearidonic acid and C23:0 tricosanoic acid. Follow-up examination with CVLT revealed positive correlations with C15:0 pentadecanoid acid, C18:3n6 gamma linoleic acid, SDA, C23:0 tricosanoic acid and negative correlations with C14:0 myristic acid and C14:1 myristolenic acids. Several tests (Trail Making Test, Stroop Dots Trail, Digit Span Test and Verbal Fluency Test) were directly correlated mainly with C14:0 myristic acid and C14:1 myristolenic acid, while corresponding negatively with C18:1 vaccinic acid, C20:3n3 cis-11-eicosatrienoic acid, C22:1/C20:1 cis11- eicosanic acid and C20:2 cis-11-eicodienoic acid. No correlations between Montreal Cognitive Assessment (MOCA) test performed on seventh day, and FFAs levels were found. Saturated fatty acids play a negative role in long-term cognitive outcomes in stroke patients. The metabolic cascade of polyunsaturated fatty acids (n3 PUFA) and the synthesis of (AA) can be involved in pathogenesis of stroke-related cognitive impairment.

[33] *Khalighfard S, Khori V, Alizadeh AM et al.* **Dual effects of atorvastatin on angiogenesis pathways in the differentiation of mesenchymal stem cells**. European journal of pharmacology 2021; 907:174281.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34217710
ABSTRACT
Atorvastatin (ATO) can improve the transplantation efficacy of mesenchymal stem cells (MSCs) after acute myocardial infarction. The present study aimed at ATO effects on the angiogenesis-signaling pathways from MSCs' differentiation to tissue angiogenesis. MSCs were first prepared from BALB/c mouse bone marrow. MTT assay was then done for the biodegradability of MSCs with the extracellular matrix. After that, the differentiation of cells into the bone and fat tissues was confirmed by Alizarin and Oil Red O staining. The extracellular matrix was then combined with the cells to the implant. Animals were intraperitoneally treated with ATO (2 and 40 mg/kg, daily) three days before cell transplantation to one week after. Finally, the assays were carried out by electron microscopy, immunocytochemistry, ELISA, Western blot, and RT-qPCR techniques. A phase-contrast microscope confirmed the morphology of cells. The cell differentiation into bone and fat tissues was confirmed by Alizarin red staining and flow cytometry, and the cell proliferation was confirmed by MTT assay. Unlike ATO 40 mg/kg group, ATO 2 mg/kg was significantly increased the CD31, eNOS, podocalyxin, von Willibrand factor, and alpha-smooth muscle actin proteins levels compared to the control group in vitro experiment. The expression of CD31 and VEGF proteins, as angiogenesis markers, and Ki-67 protein, as a proliferation marker, was significantly higher in a low dose of ATO (2 mg/kg) than that of the control group in vivo experiment. Unlike ATO 40 mg/kg, the expression levels of ERK, AKT, NF-κB, Rho, STAT3, Ets-1, HIF-1α, and VEGF proteins and genes were significantly increased in ATO 2 mg/kg compared to the control. A low dose of ATO can be a beneficial tool in the function of MSCs and their differentiation to tissue angiogenesis.

[34] *Groepenhoff F, Diez Benavente E, Boltjes A et al.* **Plasma Testosterone Levels and Atherosclerotic Plaque Gene Expression in Men With Advanced Atherosclerosis**. Frontiers in cardiovascular medicine 2021; 8:693351.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34195238
ABSTRACT

Aims: Low plasma testosterone levels have been shown to predict worse outcome in men with severe atherosclerotic disease. We hypothesized that a low plasma testosterone level affects disease risk through changes in gene expression in atherosclerotic plaques. Therefore, we studied plasma testosterone levels in relation to gene expression levels in atherosclerotic plaque tissue of men with advanced atherosclerotic disease. Methods: Plasma testosterone levels were measured in 203 men undergoing carotid endarterectomy. The corresponding atherosclerotic plaque tissue was used for RNA sequencing. First, we assessed how often the androgen receptor gene was expressed in the plaque. Second, correlations between plasma testosterone levels and pre-selected testosterone-sensitive genes were assessed. Finally, differences within the RNA expression profile of the plaque as a whole, characterized into gene regulatory networks and at individual gene level were assessed in relation to testosterone levels. Results: Testosterone plasma levels were low with a median of 11.6 nmol/L (IQR: 8.6-13.8). RNA-seq of the plaque resulted in reliable expression data for 18,850 genes to be analyzed. Within the RNA seq data, the androgen-receptor gene was expressed in 189 out of 203 (93%) atherosclerotic plaques of men undergoing carotid endarterectomy. The androgen receptor gene expression was not associated with testosterone plasma levels. There were no significant differences in gene expression of atherosclerotic plaques between different endogenous testosterone levels. This remained true for known testosterone-sensitive genes, the complete transcriptomic profile, male-specific gene co-expression modules as well as for individual genes. Conclusion: In men with severe atherosclerotic disease the androgen receptor is highly expressed in plaque tissue. However, plasma testosterone levels were neither associated with pre-selected testosterone sensitive genes, gene expression profiles nor gene regulatory networks in late-stage atherosclerotic plaques. The effect of testosterone on gene expression of the late-stage atherosclerotic plaque appears limited, suggesting that alternate mechanisms explain its effect on clinical outcomes.

[35] *Cosarca MC, Horváth E, Molnar C et al.* **Calcification patterns in femoral and carotid atheromatous plaques: A comparative morphometric study**. Experimental and therapeutic medicine 2021; 22:865.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34178138

ABSTRACT

This comparative study was designed to focus on the mineral patterns in human atherosclerotic plaques based on quantitative measurements of calcium deposits through the morphometric method. A total of 101 atherosclerotic plaques were harvested by conventional transluminal angioplasty from the carotid artery (CA) and different segments of the femoral-popliteal axis (FPA), fixed in formalin and sent for histological processing. The histological grade of the atherosclerotic plaque and the calcification pattern were evaluated, followed by a morphometric analysis of the mineral deposits. Regarding the localization, the advanced plaques (VII and VIII types) developed predominantly at the level of the superficial femoral artery (SFA) compared to the CA ($P<0.001$). This significant difference was maintained even if they were divided into low grade (IV and V) and high grade categories (VI, VII and VIII) ($P<0.05$). Compared with that in the carotid plaques, in the FPA plaques the mineralized surface increased in parallel with the narrowing of the vascular lumen diameter. The image analysis of the total pathological calcification score (pCS) showed a significant difference between the CA plaques and distal SFA (dSFA) plaques ($P=0.038$) and between the proximal SFA (pSFA) and dSFA plaques ($P=0.013$). In the case of the simple nodular pattern, calcification occupied significantly larger

areas in the plaques developed in the dSFA and popliteal artery (PA) in comparison with the CA plaques (P=0.0007 and P=0.0009). pCSs calculated in plaques with extensive calcification pattern showed a lower value in the CA vs. the pSFA plaques (P=0.004). A less pronounced, but significant difference was observed between the pCS of pSFA and dSFA plaques (P=0.017). Femoral and carotid plaques exhibited different morphology and tendency for calcification. In parallel with the narrowing of the vascular lumen diameter, the mineralized surface increased at the level of different FPA segments. These results suggest that the mechanism is site-specific, and wall structure-dependent.

[36] *Ba H, Peng H, He X et al.* **Sitosterolemia With Atherosclerosis in a Child: A Case Report**. Frontiers in pediatrics 2021; 9:668316.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34178886
ABSTRACT
Introduction: Sitosterolemia is a rare condition in children and is often misdiagnosed as familial hypercholesterolemia. Serious complications can result if not treated promptly and effectively. When pediatric patients are diagnosed with sitosterolemia, vascular, and cardiac studies are important to evaluate for the presence of atherosclerosis. Few cases of severe atherosclerotic heart disease in children with sitosterolemia have been reported, making this case worthy of presentation. Case Presentation: Here, we report a case of sitosterolemia in an 8-year-old child. The patient presented with severe hypercholesterolemia and xanthoma. He was diagnosed two and a half years prior with familial hypercholesterolemia because his father had elevated cholesterol levels. After conventional treatment, the patient was dissatisfied with lipid level control and visited our hospital for further management. Genetic tests of the patient and parents found mutations in intron 7 (NM 022436.2, c.904+1G>A) and intron 9 (NM 022436.2, C. 1324+1de1G) of ABCG5. The 7 intron mutation was from his mother, and the 9 intron mutation was from his father. The patient was diagnosed with sitosterolemia. Results: The child was treated with ezetimibe, a low plant sterol diet, and clopidogrel anticoagulant therapy. After 3 months of treatment, the blood lipid level was significantly lower. Conclusion: Genetic testing should be completed as soon as possible to avoid misdiagnosis in children with abnormally elevated hypercholesterolemia who have a family history of elevated cholesterol. In addition, clinicians should rule out great arterial lesions and be vigilant in evaluating patients for systemic arterial disease and atherosclerosis.

[37] *Amadid H, Rønn PF, Bekker-Nielsen Dunbar M et al.* **A large remaining potential in lipid-lowering drug treatment in the type 2 diabetes population: A Danish nationwide cohort study**. Diabetes Obes Metab 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34189831
ABSTRACT
AIM: To assess lipid-lowering drug (LLD) use patterns during 1996-2017 and examine lipid levels in relation to the use of LLDs and prevalent atherosclerotic cardiovascular disease (ASCVD). METHODS: Using a nationwide diabetes register, 404 389 individuals with type 2 diabetes living in Denmark during 1996-2017 were identified. Individuals were followed from 1 January 1996 or date of type 2 diabetes diagnosis until date of emigration, death or 1 January 2017. Redemptions of prescribed LLDs were ascertained from the nationwide Register of Medicinal Products Statistics. Data on lipid levels were sourced from the National Laboratory Database since 2010. LLD coverage was

calculated at any given time based on the redeemed amount and dose. Trends in lipid levels were estimated using an additive mixed-effect model. Low-density lipoprotein cholesterol (LDL-C) goal attainment was assessed based on recommended targets by the 2011, 2016 and 2019 guidelines for management of dyslipidaemias. RESULTS: LLD use has decreased since 2012 and only 55% of those with type 2 diabetes were LLD users in 2017. A decline in levels of total cholesterol and LDL-C, and an increase in triglycerides, was observed during 2010-2017. Annual mean levels of LDL-C were lower among LLD users compared with non-users (in 2017: 1.84 vs. 2.57 mmol/L). A greater fraction of LLD users achieved the LDL-C goal of less than 1.8 mmol/L compared with non-users (in 2017: 51.7% and 19%, respectively). Among LLD users with prevalent ASCVD, 26.9% and 55% had, as recommended by current 2019 European guidelines, an LDL-C level of less than 1.4 mmol/L and less than 1.8 mmol/L, respectively, in 2017. CONCLUSIONS: LLD use and LDL-C levels are far from optimal in the Danish type 2 diabetes population and improvement in LLD use could reduce ASCVD events.

[38] *Stasi A, Franzin R, Fiorentino M et al.* **Multifaced Roles of HDL in Sepsis and SARS-CoV-2 Infection: Renal Implications**. International journal of molecular sciences 2021; 22.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34205975
ABSTRACT
High-density lipoproteins (HDLs) are a class of blood particles, principally involved in mediating reverse cholesterol transport from peripheral tissue to liver. Omics approaches have identified crucial mediators in the HDL proteomic and lipidomic profile, which are involved in distinct pleiotropic functions. Besides their role as cholesterol transporter, HDLs display anti-inflammatory, anti-apoptotic, anti-thrombotic, and anti-infection properties. Experimental and clinical studies have unveiled significant changes in both HDL serum amount and composition that lead to dysregulated host immune response and endothelial dysfunction in the course of sepsis. Most SARS-Coronavirus-2-infected patients admitted to the intensive care unit showed common features of sepsis disease, such as the overwhelmed systemic inflammatory response and the alterations in serum lipid profile. Despite relevant advances, episodes of mild to moderate acute kidney injury (AKI), occurring during systemic inflammatory diseases, are associated with long-term complications, and high risk of mortality. The multi-faceted relationship of kidney dysfunction with dyslipidemia and inflammation encourages to deepen the clarification of the mechanisms connecting these elements. This review analyzes the multifaced roles of HDL in inflammatory diseases, the renal involvement in lipid metabolism, and the novel potential HDL-based therapies.

[39] *Sagris M, Theofilis P, Antonopoulos AS et al.* **Inflammatory Mechanisms in COVID-19 and Atherosclerosis: Current Pharmaceutical Perspectives**. International journal of molecular sciences 2021; 22.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34205487
ABSTRACT
Coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been associated with excess mortality worldwide. The cardiovascular system is the second most common target of SARS-CoV-2, which leads to severe complications, including acute myocardial injury, myocarditis, arrhythmias, and venous thromboembolism, as well as other major thrombotic events because of direct endothelial injury and an excessive systemic inflammatory

response. This review focuses on the similarities and the differences of inflammatory pathways involved in COVID-19 and atherosclerosis. Anti-inflammatory agents and immunomodulators have recently been assessed, which may constitute rational treatments for the reduction of cardiovascular events in both COVID-19 and atherosclerotic heart disease.

[40] *Poznyak AV, Bharadwaj D, Prasad G et al.* **Renin-Angiotensin System in Pathogenesis of Atherosclerosis and Treatment of CVD**. International journal of molecular sciences 2021; 22.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34206708

ABSTRACT

Atherosclerosis has complex pathogenesis, which involves at least three serious aspects: inflammation, lipid metabolism alterations, and endothelial injury. There are no effective treatment options, as well as preventive measures for atherosclerosis. However, this disease has various severe complications, the most severe of which is cardiovascular disease (CVD). It is important to note, that CVD is among the leading causes of death worldwide. The renin-angiotensin-aldosterone system (RAAS) is an important part of inflammatory response regulation. This system contributes to the recruitment of inflammatory cells to the injured site and stimulates the production of various cytokines, such as IL-6, TNF-a, and COX-2. There is also an association between RAAS and oxidative stress, which is also an important player in atherogenesis. Angiotensin-II induces plaque formation at early stages, and this is one of the most crucial impacts on atherogenesis from the RAAS. Importantly, while stimulating the production of ROS, Angiotensin-II at the same time decreases the generation of NO. The endothelium is known as a major contributor to vascular function. Oxidative stress is the main trigger of endothelial dysfunction, and, once again, links RAAS to the pathogenesis of atherosclerosis. All these implications of RAAS in atherogenesis lead to an explicable conclusion that elements of RAAS can be promising targets for atherosclerosis treatment. In this review, we also summarize the data on treatment approaches involving cytokine targeting in CVD, which can contribute to a better understanding of atherogenesis and even its prevention.

[41] *Poznyak AV, Bharadwaj D, Prasad G et al.* **Anti-Inflammatory Therapy for Atherosclerosis: Focusing on Cytokines**. International journal of molecular sciences 2021; 22.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34209109

ABSTRACT

Atherosclerosis is a well-known global health problem. Despite the high prevalence of the disease, numerous aspects of pathogenesis remain unclear. Subsequently, there are still no cure or adequate preventive measures available. Atherogenesis is now considered a complex interplay between lipid metabolism alterations, oxidative stress, and inflammation. Inflammation in atherogenesis involves cellular elements of both innate (such as macrophages and monocytes) and adaptive immunity (such as B-cells and T-cells), as well as various cytokines cascades. Because inflammation is, in general, a well-investigated therapeutic target, and strategies for controlling inflammation have been successfully used to combat a number of other diseases, inflammation seems to be the preferred target for the treatment of atherosclerosis as well. In this review, we summarized data on targeting the most studied inflammatory molecular targets, CRP, IL-1β, IL-6, IFN-γ, and TNF-α. Studies in animal models have shown the efficacy of anti-inflammatory therapy, while clinical studies revealed the incompetence of existing data, which blocks the development of an effective atheroprotective

drug. However, all data on cytokine targeting give evidence that anti-inflammatory therapy can be a part of a complex treatment.

[42] *Okoro EU*. **TNFα-Induced LDL Cholesterol Accumulation Involve Elevated LDLR Cell Surface Levels and SR-B1 Downregulation in Human Arterial Endothelial Cells**. International journal of molecular sciences 2021; 22.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34207810
ABSTRACT
Excess lipid droplets are frequently observed in arterial endothelial cells at sites of advanced atherosclerotic plaques. Here, the role of tumor necrosis factor alpha (TNFα) in modulating the low-density lipoprotein (LDL) content in confluent primary human aortic endothelial cells (pHAECs) was investigated. TNFα promoted an up to 2 folds increase in cellular cholesterol, which was resistant to ACAT inhibition. The cholesterol increase was associated with increased (125)I-LDL surface binding. Using the non-hydrolysable label, DiI, TNFα could induce a massive increase in DiI-LDL by over 200 folds. The elevated intracellular DiI-LDL was blocked with excess unlabeled LDL and PCSK9, but not oxidized LDL (oxLDL), or apolipoprotein (apoE) depletion. Moreover, the TNFα-induced increase of LDL-derived lipids was elevated through lysosome inhibition. Using specific LDLR antibody, the DiI-LDL accumulation was reduced by over 99%. The effects of TNFα included an LDLR cell surface increase of 138%, and very large increases in ICAM-1 total and surface proteins, respectively. In contrast, that of scavenger receptor B1 (SR-B1) was reduced. Additionally, LDLR antibody bound rapidly in TNFα-treated cells by about 30 folds, inducing a migrating shift in the LDLR protein. The effect of TNFα on DiI-LDL accumulation was inhibited by the antioxidant tetramethythiourea (TMTU) dose-dependently, but not by inhibitors against NF-κB, stress kinases, ASK1, JNK, p38, or apoptosis caspases. Grown on Transwell inserts, TNFα did not enhance apical to basolateral LDL cholesterol or DiI release. It is concluded that TNFα promotes LDLR functions through combined increase at the cell surface and SR-B1 downregulation.

[43] *Lee MC, Peng TR, Chen BL et al.* **Effects of various statins on depressive symptoms: A network meta-analysis**. Journal of affective disorders 2021; 293:205-213.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34217957
ABSTRACT
BACKGROUND: Previous studies have indicated that statins can reduce the severity of depressive symptoms. However, the optimal choice of statin remains unclear. Therefore, we conducted a network meta-analysis to determine the optimal statin for treating depression. METHOD: We performed a pairwise and network meta-analysis by searching the PubMed, Embase, and Cochrane Library databases on October 29th, 2020. Eligible studies were randomized controlled trials that reported on changes in depressive symptoms. The Cochrane Collaboration tool was used to assess risk of bias. We tested for possible inconsistency globally by using a χ(2)-test and locally by calculating inconsistency factors for each comparison in closed loops. The ranking probabilities of being at each possible rank for each intervention were estimated. Comparison-adjusted funnel plots were obtained to assess publication bias. Sensitivity analysis was also performed. RESULTS: We identified 13 studies that matched our inclusion criteria. The risks of bias were mostly low. None of the global or local tests found significance. Compared with placebo, atorvastatin significantly reduced the severity of depressive symptoms (mean difference -3.46, 95% confidence interval -5.26 to -1.67).

Atorvastatin had the first and second rank with probabilities of 44.9% and 39.0%, respectively. Comparison-adjusted funnel plots revealed no significant publication bias. LIMITATIONS: Low similarity of included studies and a relative large treatment effect of a single study were observed. CONCLUSIONS: In this first network meta-analysis, atorvastatin, with high intensity and a lipophilic effect, was identified as the optimal choice of statin for treating depression.

[44] *Kotlyarov S, Kotlyarova A*. **The Role of ABC Transporters in Lipid Metabolism and the Comorbid Course of Chronic Obstructive Pulmonary Disease and Atherosclerosis**. International journal of molecular sciences 2021; 22.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34201488
ABSTRACT
Chronic obstructive pulmonary disease (COPD) ranks among the leading causes of morbidity and mortality worldwide. COPD rarely occurs in isolation and is often combined with various diseases. It is considered that systemic inflammation underlies the comorbid course of COPD. The data obtained in recent years have shown the importance of violations of the cross-links of lipid metabolism and the immune response, which are links in the pathogenesis of both COPD and atherosclerosis. The role of lipid metabolism disorders in the pathogenesis of the comorbid course of COPD and atherosclerosis and the participation of ATP-binding cassette (ABC) transporters in these processes is discussed in this article. It is known that about 20 representatives of a large family of ABC transporters provide lipid homeostasis of cells by moving lipids inside the cell and in its plasma membrane, as well as removing lipids from the cell. It was shown that some representatives of the ABC-transporter family are involved in various links of the pathogenesis of COPD and atherosclerosis, which can determine their comorbid course.

[45] *Halperin JL, Chen H, Olin JW*. **Antithrombotic Therapy to Reduce Mortality in Patients With Atherosclerosis: 2 Pathways to a Single Goal**. Journal of the American College of Cardiology 2021; 78:24-26.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34210410
ABSTRACT

[46] *Gonzalez-Santos LE, Oliva R, Jimeno C et al.* **Executive Summary of the 2020 Clinical Practice Guidelines for the Management of Dyslipidemia in the Philippines**. J ASEAN Fed Endocr Soc 2021; 36:5-11.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34177082
ABSTRACT
Dyslipidemia is a cardiovascular risk factor that is increasing in prevalence in the country. The need to treat and manage elevated cholesterol levels, both pharmacologic and non-pharmacologic, is of utmost importance. Different medical societies and groups bonded together to formulate the 2020 Philippine Clinical Practice Guidelines for dyslipidemia. The group raised nine clinical questions that are important in dyslipidemia management. A technical working group analyzed the clinical questions dealing with non-pharmacologic management, primary prevention for both non-diabetic and individuals with diabetes, familial hypercholesterolemia, secondary prevention, adverse events of statins and the use of other lipid parameters as measurement of risk for cardiovascular disease. Randomized controlled trials and meta-analyses were included in the GRADE-PRO analysis to come

up with the statements answering the clinical questions. The statements were presented to a panel consisting of government agencies, members of the different medical societies, and private institutions, and the statements were voted upon to come up with the final statements of the 2020 practice guidelines. The 2020 CPG is aimed for the Filipino physician to confidently care for the individual with dyslipidemia and eventually lower his risk for cardiovascular disease.

[47] *Eikelboom JW, Bhatt DL, Fox KAA et al.* **Mortality Benefit of Rivaroxaban Plus Aspirin in Patients With Chronic Coronary or Peripheral Artery Disease**. Journal of the American College of Cardiology 2021; 78:14-23.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34210409

ABSTRACT

BACKGROUND: The combination of 2.5 mg rivaroxaban twice daily and 100 mg aspirin once daily compared with 100 mg aspirin once daily reduces major adverse cardiovascular (CV) events in patients with chronic coronary artery disease (CAD) or peripheral artery disease (PAD). OBJECTIVES: The aim of this work was to report the effects of the combination on overall and cause-specific mortality. METHODS: The COMPASS trial enrolled 27,395 patients of whom 18,278 were randomized to the combination (n = 9,152) or aspirin alone (n = 9,126). Deaths were adjudicated by a committee blinded to treatment allocation. Previously identified high-risk baseline features were polyvascular disease, chronic kidney disease, mild or moderate heart failure, and diabetes. RESULTS: During a median of 23 months of follow-up (maximum 47 months), 313 patients (3.4%) allocated to the combination and 378 patients (4.1%) allocated to aspirin alone died (hazard ratio [HR]: 0.82; 95% confidence interval [CI]: 0.71-0.96; P = 0.01). Compared with aspirin, the combination reduced CV death (160 [1.7%] vs 203 [2.2%]; HR: 0.78; 95% CI: 0.64-0.96; P = 0.02) but not non-CV death. There were fewer deaths following MI, stroke, and CV procedures, as well as fewer sudden cardiac, other, and unknown causes of CV deaths and coronary heart disease deaths. Patients with 0, 1, 2, and 3 or 4 high-risk features at baseline had 4.2, 4.8, 25.0, and 53.9 fewer deaths, respectively, per 1000 patients treated for 30 months. CONCLUSIONS: The combination of rivaroxaban and aspirin compared with aspirin reduced overall and CV mortality with consistent reductions in cause specific CV mortality in patients with chronic CAD or PAD. The absolute mortality benefits are greater with increasing baseline risk. (Cardiovascular Outcomes for People Using Anticoagulant Strategies [COMPASS]; NCT01776424).

[48] *Dabravolski SA, Bezsonov EE, Baig MS et al.* **Mitochondrial Lipid Homeostasis at the Crossroads of Liver and Heart Diseases**. International journal of molecular sciences 2021; 22.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34203309

ABSTRACT

The prevalence of NAFLD (non-alcoholic fatty liver disease) is a rapidly increasing problem, affecting a huge population around the globe. However, CVDs (cardiovascular diseases) are the most common cause of mortality in NAFLD patients. Atherogenic dyslipidemia, characterized by plasma hypertriglyceridemia, increased small dense LDL (low-density lipoprotein) particles, and decreased HDL-C (high-density lipoprotein cholesterol) levels, is often observed in NAFLD patients. In this review, we summarize recent genetic evidence, proving the diverse nature of metabolic pathways involved in NAFLD pathogenesis. Analysis of available genetic data suggests that the altered operation of fatty-acid β-oxidation in liver mitochondria is the key process, connecting NAFLD-

mediated dyslipidemia and elevated CVD risk. In addition, we discuss several NAFLD-associated genes with documented anti-atherosclerotic or cardioprotective effects, and current pharmaceutical strategies focused on both NAFLD treatment and reduction of CVD risk.

[49] *Tada H, Hori M, Matsuki K et al.* **Achilles Tendon Thickness Assessed by X-ray Predicting a Pathogenic Mutation in Familial Hypercholesterolemia Gene**. Journal of atherosclerosis and thrombosis 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34193720
ABSTRACT
AIM: The 2017 Japan Atherosclerosis Society (JAS) familial hypercholesterolemia (FH) criteria adopt a cut-off value of ≥ 9 mm of Achilles tendon thickness (ATT) detected by X-ray as one of the three key items. This threshold was determined based on an old data evaluating the ATT of 36 non-FH individuals that was published in 1977. Although the specificity of these clinical criteria is extremely high due to a strict threshold, there are a significant number of patients with FH whose ATT ＜9 mm. We aimed to determine a cut-off value of ATT detected by X-ray to differentiate FH and non-FH based on genetic diagnosis. METHODS: The individuals (male/female=486/501) with full assessments of genetic analyses for FH-genes (LDLR and PCSK9), serum lipids, and ATT detected by X-ray at the Kanazawa University Hospital and National Cerebral and Cardiovascular Center Research Institute were included in this study. Receiver operating characteristic (ROC) analyses were conducted to determine a better cut-off value of ATT that predicts the pathogenic mutation of FH. RESULTS: The ROC analyses revealed that the best cut-off values of ATT are 7.6 mm for male and 7.0 mm for female, with the sensitivities/specificities of 0.83/0.83 for male and 0.86/0.85 for female, respectively. If the thresholds of ATT of 8.0/7.5 mm and 7.5/7.0 mm were applied to the diagnosis of male/female FH, the sensitivities/specificities predicting the pathogenic mutation of FH by the 2017 JAS FH clinical criteria would be 0.82/0.90 and 0.85/0.88, respectively. CONCLUSIONS: These results suggest that the cut-off value of ATT detected by X-ray is obviously lower than 9.0 mm, which was adopted by the 2017 JAS FH clinical criteria.

[50] *Setny M, Jankowski P, Krzykwa A et al.* **Management of Dyslipidemia in Women and Men with Coronary Heart Disease: Results from POLASPIRE Study**. Journal of clinical medicine 2021; 10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34208351
ABSTRACT
Cardiovascular diseases (CVDs) are the leading cause of death in Poland. Starting from 1992, a gradual decrease in mortality due to CVDs has been observed, which is less noticeable in women. Following this notion, we assessed sex differences in the implementation of ESC recommendations regarding lipid control and the use of statins as part of secondary CVDs prevention in 1236 patients with acute coronary syndrome or elective coronary revascularization within the last 6-24 months. During hospitalization women had more frequently abnormal TC levels than men (p = 0.035), with overall higher TC levels (p = 0.009) and lower HDL-C levels (p = 0.035). In the oldest group, they also had more frequently elevated LDL-C levels (p = 0.033). Similar relationships were found during the follow-up visit. In addition, women less often achieved the secondary lipid therapeutic goal for non-HDL-C (p = 0.009). At discharge from hospital women were less frequently prescribed statins (p = 0.001), which included high-intensity statins (p = 0.002). At the follow-up visit the use of high-intensity

statins was still less frequent in women (p = 0.02). We conclude that women generally have less optimal lipid profiles than men and are less likely to receive high-intensity statins. There is a need for more organized care focused on the management of risk factors.

[51] *Roy-Vallejo E, Sánchez Purificación A, Torres Peña JD et al.* **Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers Withdrawal Is Associated with Higher Mortality in Hospitalized Patients with COVID-19**. Journal of clinical medicine 2021; 10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34204014

ABSTRACT

Our main aim was to describe the effect on the severity of ACEI (angiotensin-converting enzyme inhibitor) and ARB (angiotensin II receptor blocker) during COVID-19 hospitalization. A retrospective, observational, multicenter study evaluating hospitalized patients with COVID-19 treated with ACEI/ARB. The primary endpoint was the incidence of the composite outcome of prognosis (IMV (invasive mechanical ventilation), NIMV (non-invasive mechanical ventilation), ICU admission (intensive care unit), and/or all-cause mortality). We evaluated both outcomes in patients whose treatment with ACEI/ARB was continued or withdrawn. Between February and June 2020, 11,205 patients were included, mean age 67 years (SD = 16.3) and 43.1% female; 2162 patients received ACEI/ARB treatment. ACEI/ARB treatment showed lower all-cause mortality (p < 0.0001). Hypertensive patients in the ACEI/ARB group had better results in IMV, ICU admission, and the composite outcome of prognosis (p < 0.0001 for all). No differences were found in the incidence of major adverse cardiovascular events. Patients previously treated with ACEI/ARB continuing treatment during hospitalization had a lower incidence of the composite outcome of prognosis than those whose treatment was withdrawn (RR 0.67, 95%CI 0.63-0.76). ARB was associated with better survival than ACEI (HR 0.77, 95%CI 0.62-0.96). ACEI/ARB treatment during COVID-19 hospitalization was associated with protection on mortality. The benefits were greater in hypertensive, those who continued treatment, and those taking ARB.

[52] *Rogula S, Błażejowska E, Gąsecka A et al.* **Inclisiran-Silencing the Cholesterol, Speaking up the Prognosis**. Journal of clinical medicine 2021; 10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34199468

ABSTRACT

The reduction of circulating low-density lipoprotein-cholesterol (LDL-C) is a primary target in cardiovascular risk reduction due to its well-established benefits in terms of decreased mortality. Despite the use of statin therapy, 10%-20% of high- and very-high-risk patients do not reach their LDL-C targets. There is an urgent need for improved strategies to manage dyslipidemia, especially among patients with homozygous familial hypercholesterolemia, but also in patients with established cardiovascular disease who fail to achieve LDL goals despite combined statin, ezetimibe, and PCSK9 inhibitor (PCSK9i) therapy. Inclisiran is a disruptive, first-in-class small interfering RNA (siRNA)-based therapeutic developed for the treatment of hypercholesterolemia that inhibits proprotein convertase subtilisin-kexin type 9 (PCSK9) synthesis, thereby upregulating the number of LDL receptors on the hepatocytes, thus lowering the plasma LDL-C concentration. Inclisiran decreases the LDL-C levels by over 50% with one dose every 6 months, making it a simple and well-tolerated treatment strategy. In this review, we summarize the general information regarding (i) the role of LDL-C in atherosclerotic cardiovascular disease, (ii) data regarding the role of PCSK9 in cholesterol metabolism, (iii)

pleiotropic effects of PCSK9, and (iv) the effects of PCSK9 silencing. In addition, we focus on inclisiran, in terms of its (i) mechanism of action, (ii) biological efficacy and safety, (iii) results from the ORION trials, (iv) benefits of its combination with statins, and (v) its potential future role in atherosclerotic cardiovascular disease.

[53] *Patel D, Busch R*. **Omega-3 Fatty Acids and Cardiovascular Disease: A Narrative Review for Pharmacists**. Journal of cardiovascular pharmacology and therapeutics 2021:10742484211023715.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34191622

ABSTRACT

BACKGROUND: Atherosclerotic cardiovascular disease is a significant cause of morbidity and mortality worldwide. While use of statin therapy has improved management of lipids, an unmet need in reducing residual atherosclerotic cardiovascular disease risk and ischemic events persists. We provide an overview of the pharmacology of omega-3 fatty acids, omega-3 fatty acid cardiovascular outcomes trials, landmark clinical data and pharmacology of icosapent ethyl (a stable and highly purified ethyl ester of eicosapentaenoic acid), and the critical differences between fish oil supplements and prescription omega-3 fatty acids. METHOD: A PubMed literature review was conducted in April 2020 to identify articles discussing omega-3 fatty acid cardiovascular outcomes trials, pharmacology of icosapent ethyl, and the evaluation of fish oil dietary supplements and prescription omega-3 fatty acids. RESULTS: Both eicosapentaenoic acid and docosahexaenoic acid have been widely associated with positive health benefits; however, data are inconsistent regarding the benefit of combination eicosapentaenoic acid and docosahexaenoic acid in patients with cardiovascular disease. Eicosapentaenoic acid, and specifically icosapent ethyl, has demonstrated atherosclerotic cardiovascular disease risk reduction among statin-treated patients. Important clinical differences exist between dietary supplement and prescription omega-3 fatty acid products. CONCLUSIONS: As research regarding the optimal management of dyslipidemia continues, additional therapy beyond statins is necessary to reduce atherosclerotic cardiovascular disease risk. In large cardiovascular outcomes trials, eicosapentaenoic acid has demonstrated cardiovascular benefit. Icosapent ethyl possesses a favorable efficacy and safety profile and should be considered as an adjunct to statin therapy to reduce ischemic event risk.

[54] *Izkhakov E, Shacham Y, Serebro M et al.* **The Effect of the PCSK9 Inhibitor Evolocumab on Aldosterone Secretion among High Cardiovascular Risk Patients: A Pilot Study**. Journal of clinical medicine 2021; 10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34198795

ABSTRACT

Elevated low-density lipoprotein (LDL) cholesterol is one of the leading causes of cardiovascular disease. Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors reduce LDL cholesterol levels with subsequent reductions in cardiovascular morbidity. Elevated aldosterone levels are also associated with a greater risk of cardiovascular morbidity. There are currently no published data on the impact of PCSK9 inhibitor monotherapy on the secretion of aldosterone. The aim of this study was to examine the effect of monotherapy with the PSCK9 inhibitor evolocumab on the lipid profile and aldosterone secretion level in high-risk cardiovascular patients. Lipid profile, sodium, potassium, aldosterone, cortisol, plasma renin activity, and adrenocorticotropic hormone (ACTH) levels were analyzed at baseline and after 3 months of evolocumab therapy. Each participant underwent a 250

mcg ACTH stimulation test upon study entry. Eight women and seven men were included in the study. Their median total cholesterol, LDL cholesterol, lipoprotein (a), apolipoprotein B100, and baseline and stimulated aldosterone levels were significantly lower after 3 months of evolocumab therapy. These heretofore unreported findings indicate that reductions in unstimulated and stimulated aldosterone secretion under evolocumab therapy could be associated with reductions in cardiovascular events, a possibility that warrants further investigation.

[55] *Handayani W, Suharjono, Yogiarto M*. **Analysis of HMGB-1 level before and after providing atorvastatin standard therapy in coronary artery disease patients with type-2 diabetes mellitus compared to without type-2 diabetes mellitus**. Journal of basic and clinical physiology and pharmacology 2021; 32:439-446.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34214372
ABSTRACT
OBJECTIVES: Coronary artery disease (CAD) is one of the main causes of death from cardiovascular disease, because heart attacks result in atherosclerosis which causes narrowing of the arteries. Atorvastatin has a pleiotropic effect as anti-inflammatory through one of the target levels of High Mobility Group Box-1 (HMGB-1). This prospective observational study aimed to analyze the effect of atorvastatin on serum HMGB-1 levels in CAD. METHODS: Samples were collected from prospective observation pre-post study in May-July 2018 with consecutive sampling method. Serum HMGB-1 levels were measured in patients with CAD who were given atorvastatin for CAD with type-2 diabetes mellitus compared without type-2 diabetes mellitus in a patient ward. Blood was collected on admission day and before the patient left the hospital. After centrifugation, serum samples were stored at -80 °C before measurement. We used an ELISA kit (IBL International) to determine HMGB-1 concentrations. This research protocol has been approved by the Ethical Committee of Dr. Soetomo General Hospital, Surabaya. RESULTS: We enrolled 38 patients and divided them into two groups which 19 patients on CAD with type-2 diabetes mellitus and 19 patients without diabetes mellitus. Serum HMGB-1 levels in CAD with type-2 diabetes mellitus were increased significantly ($p = 0.049$) and not significantly decreased in CAD without type-2 diabetes mellitus ($p = 0.480$). The HMGB-1 level was not significantly different between the two groups ($p = 0.210$). CONCLUSIONS: HMGB-1 levels after providing atorvastatin in CAD with type-2 diabetes mellitus increased significantly, meanwhile, in CAD without type-2 diabetes mellitus did not decrease significantly. The HMGB-1 level was not significantly different between the two groups. Longer time and more point for the collected sample needed for further research.

[56] *Dunn SL, Vera DL, Weaver KF, Garcia JV*. **Relationships between inflammatory and metabolic markers, exercise, and body composition in young individuals**. J Clin Transl Res 2021; 7:289-296.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34179543
ABSTRACT
BACKGROUND AND AIMS: Physical exercise may help combat disease and elicits a possible "protective" anti-inflammatory effect on the body. Inflammatory cytokines, C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-α (TNFα), along with transcription factor, nuclear factor-kappa B (NFκB) in young (n=16, 21.1±2.1 years) individuals were examined in a cross-sectional descriptive study, to assess the effects of chronic stimulation on their expression and relationship with

health parameters. METHODS: Fasting venous whole blood and lipid levels along with body composition measurements were obtained from young, healthy, endurance-trained NCAA Division III student-athletes and untrained individuals. Assays (ELISA) were conducted to analyze fasting plasma (CRP, IL-6, and TNFα) and isolated lymphocyte NF-κB activation (lymphocytes were isolated from whole blood samples through differential centrifugation and Ficoll-Paque). A Spearman's rank order correlation coefficient was used for associations between variables and a regression analysis was performed to determine which measurement accounted for the inflammation in this young and apparently healthy population. RESULTS: While the inflammatory markers were not associated with each other, CRP levels were associated with body composition and following regression analyses, body fat percentage (P>0.05) was a significant factor for elevated CRP. CONCLUSIONS: Chronic physical exercise eliciting lower body fat percentages in young adults may have a positive protective impact through anti-inflammatory status, minimizing disease risk in a young population. RELEVANCE FOR PATIENTS: Chronic physically active young adult patients may exhibit less inflammation and lower body fat levels which may decrease their risk for chronic disease.

[57] *Dai D, Shen Y, Lu J et al.* **Association between visit-to-visit variability of glycated albumin and diabetic retinopathy among patients with type 2 diabetes - A prospective cohort study**. Journal of diabetes and its complications 2021; 35:107971.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34187717
ABSTRACT
AIM: There is a paucity of studies regarding the association between long-term glycemic variability with the risk of diabetic retinopathy (DR) in patients with type 2 diabetes. Therefore, the purpose of this study is to explore the association of glycated albumin (GA) variability and HbA1c variability with the risk of DR in patients with type 2 diabetes. METHODS: This prospective cohort study included 315 inpatients with type 2 diabetes (191 males and 124 females) with at least 3 measurements of GA and HbA1c within 2years prior to the baseline investigation. Different GA and HbA1c variability markers were calculated, including CV, variability independent of the mean (VIM), and the average real variability (ARV). Cox proportional hazard regression models were used to explore the association between visit-to-visit variability of GA and HbA1c and the risk of DR. RESULTS: After an average follow-up of 3.42years, 81 patients developed incident DR. Multivariable-adjusted (diabetes duration, smoking status, systolic blood pressure, albumin to creatinine ratio, triglycerides, using fibrates, and mean HbA1c) hazard ratios of DR associated with each unit increase in GA-CV, GA-VIM, and GA-ARV were 1.05 (95% CI 1.02-1.09), 1.69 (95% CI 1.24-2.32), and 1.13 (95%CI 1.04-1.23), respectively. However, there was no significant association between visit-to-visit HbA1c variability and the risk of DR. CONCLUSIONS: The present study indicated that visit-to-visit variability of GA can predict the risk of incident DR in patients with type 2 diabetes, and the prediction ability is independent of the average HbA1c levels.

[58] *Afanasieva OI, Filatova AY, Arefieva TI et al.* **The Association of Lipoprotein(a) and Circulating Monocyte Subsets with Severe Coronary Atherosclerosis**. Journal of cardiovascular development and disease 2021; 8.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34206012
ABSTRACT

BACKGROUND AND AIMS: Chronic inflammation associated with the uncontrolled activation of innate and acquired immunity plays a fundamental role in all stages of atherogenesis. Monocytes are a heterogeneous population and each subset contributes differently to the inflammatory process. A high level of lipoprotein(a) (Lp(a)) is a proven cardiovascular risk factor. The aim of the study was to investigate the association between the increased concentration of Lp(a) and monocyte subpopulations in patients with a different severity of coronary atherosclerosis. METHODS: 150 patients (124 males) with a median age of 60 years undergoing a coronary angiography were enrolled. Lipids, Lp(a), autoantibodies, blood cell counts and monocyte subpopulations (classical, intermediate, non-classical) were analyzed. RESULTS: The patients were divided into two groups depending on the Lp(a) concentration: normal Lp(a) < 30 mg/dL (n = 82) and hyperLp(a) ≥ 30 mg/dL (n = 68). Patients of both groups were comparable by risk factors, autoantibody levels and blood cell counts. In patients with hyperlipoproteinemia(a) the content (absolute and relative) of non-classical monocytes was higher (71.0 (56.6; 105.7) vs. 62.2 (45.7; 82.4) 10(3)/mL and 17.7 (13.0; 23.3) vs. 15.1 (11.4; 19.4) %, respectively, $p < 0.05$). The association of the relative content of non-classical monocytes with the Lp(a) concentration retained a statistical significance when adjusted for gender and age ($r = 0.18$, $p = 0.03$). The severity of coronary atherosclerosis was associated with the Lp(a) concentration as well as the relative and absolute ($p < 0.05$) content of classical monocytes. The high content of non-classical monocytes (OR = 3.5, 95% CI 1.2-10.8) as well as intermediate monocytes (OR = 8.7, 2.5-30.6) in patients with hyperlipoproteinemia(a) were associated with triple-vessel coronary disease compared with patients with a normal Lp(a) level and a low content of monocytes. CONCLUSION: Hyperlipoproteinemia(a) and a decreased quantity of classical monocytes were associated with the severity of coronary atherosclerosis. The expansion of CD16+ monocytes (intermediate and non-classical) in the presence of hyperlipoproteinemia(a) significantly increased the risk of triple-vessel coronary disease.

[59] *Zvizdić F, Begić E, Dilić M et al.* **Effect of atorvastatin on systolic and diastolic function in patients with heart failure with reduced ejection fraction (HFrEF)**. Medicinski glasnik : official publication of the Medical Association of Zenica-Doboj Canton, Bosnia and Herzegovina 2021; 18.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34212706

ABSTRACT

Aim To investigate the benefit of high-dose lipophilic statin therapy on cardiac remodelling, function and progression of heart failure (HF) in patients with ischemic heart disease. Methods A total of 80 patients with ischemic HF diagnosis were followed during 6 months, and they were divided in two groups. First group (n=40) was treated by high-dose lipophilic statin therapy (atorvastatin 40 mg) and conventional therapy for HF, while the second group (n=40) had no atorvastatin in the therapy. Results In the beginning of study, from all of the observed parameters, only the ratio of flow rates in early and late diastole (E/A ratio) differed between the test groups (p=0.007). After six months, a statistically significant increase in left ventricular end-diastolic diameter (LVIDD) in patients who had not been treated with atorvastatin was found. In the patients treated with atorvastatin, there was a significant reduction in basal right ventricle diameter in diastole and systole (p<0.001 and p<0.001, respectively), and in tricuspid annular plane systolic excursion (TAPSE) (p<0.001); there was a reduction in LVIDD (p<0.001), and an increase of ejection fraction of the left ventricle according to Teicholtz and Simpson (p<0.001 and p<0.001, respectively). Also, there was an increase of deceleration time of early diastolic velocity (DTE) (p<0.05) and a decrease of isovolumic relaxation

time (IVRT) (p<0.001). Conclusion The reduction in the right and left ventricle diameters was noted after the six-month atorvastatin therapy. Atorvastatin in the therapy resulted in increased EFLV and better systolic function and should be a part of a therapeutic modality of HF.

[60] *Tse G, Zhou J, Lee S et al.* **Relationship between angiotensin-converting enzyme inhibitors or angiotensin receptor blockers and COVID-19 incidence or severe disease**. Journal of hypertension 2021; 39:1717-1724.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34188006
ABSTRACT
BACKGROUND: Angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) may be associated with higher susceptibility of COVID-19 infection and adverse outcomes. We compared ACEI/ARB use and COVID-19 positivity in a case-control design, and severity in COVID-19 positive patients. METHODS: Consecutive patients who attended Hong Kong's public hospitals or outpatient clinics between 1 January and 28 July 2020 for COVID-19 real time-PCR (RT-PCR) tests were included. Baseline demographics, past comorbidities, laboratory tests and use of different medications were compared between COVID-19 positive and negative patients. Severe endpoints for COVID-19 positive patients were 28-day mortality, need for intensive care admission or intubation. RESULTS: This study included 213788 patients (COVID-19 positive: n=2774 patients; negative: n=211014). In total, 162 COVID-19 positive patients (5.83%) met the severity outcome. The use of ACEI/ARB was significantly higher amongst cases than controls (n=156/2774, 5.62 vs. n=6708/211014, 3.17%; P<0.0001). Significant univariate predictors of COVID-19 positivity and severe COVID-19 disease were older age, higher Charlson score, comorbidities, use of ACEI/ARB, antidiabetic, lipid-lowering, anticoagulant and antiplatelet drugs and laboratory tests (odds ratio >1, P<0.05). The relationship between the use of ACEI/ARB and COVID-19 positivity or severe disease remained significant after multivariable adjustment. No significant differences in COVID-19 positivity or disease severity between ACEI and ARB use were observed (P>0.05). CONCLUSION: There was a significant relationship between ACEI/ARB use and COVID-19 positivity and severe disease after adjusting for significant confounders.

[61] *Tilinca MC, Tiuca RA, Burlacu A, Varga A*. **A 2021 Update on the Use of Liraglutide in the Modern Treatment of 'Diabesity': A Narrative Review**. Medicina (Kaunas, Lithuania) 2021; 57.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34209532
ABSTRACT
Obesity and type 2 diabetes mellitus have become a significant public health problem in the past decades. Their prevalence is increasing worldwide each year, greatly impacting the economic and personal aspects, mainly because they frequently coexist, where the term "diabesity" may be used. The drug class of glucagon-like peptide 1 receptor agonists (GLP-1 RAs) is one of the most modern therapy options in managing these metabolic disorders. This review focuses on the effects of liraglutide, a long-acting GLP-1 RA, in diabesity and non-diabetic excess weight. This drug class improves glycemic control by enhancing insulin secretion from the beta-pancreatic cells and inhibiting glucagon release. Furthermore, other effects include slowing gastric emptying, increasing postprandial satiety, and reducing the appetite and food consumption by influencing the central nervous system, with weight reduction effects. It also reduces cardiovascular events and has positive effects on blood pressure and lipid profile. A lower-dose liraglutide (1.2 or 1.8 mg/day) is used in

patients with diabetes, while the higher dose (3.0 mg/day) is approved as an anti-obesity drug. In this review, we have summarized the role of liraglutide in clinical practice, highlighting its safety and efficacy as a glucose-lowering agent and a weight-reduction drug in patients with and without diabetes.

[62] *Tarar ZI, Zafar MU, Ghous G et al.* **Pravastatin-Induced Acute Pancreatitis: A Case Report and Literature Review**. Journal of investigative medicine high impact case reports 2021; 9:23247096211028386.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34180257
ABSTRACT
Pancreatitis is inflammation of pancreas associated most commonly with chronic alcoholism and gallstones. Other less common causes of pancreatitis are hyperlipidemia, infections, surgery, trauma, post endoscopic retrograde cholangiopancreatography, and drugs. Drugs are now increasingly recognized as a cause of pancreatitis, and high suspicion and exclusion of other most common causes is required before considering drug-induced pancreatitis. There are few case reports of acute pancreatitis in the literature after statin use, but out of these, only 3 are after starting pravastatin. We are reporting a case of 49-year-old male who presented with nausea, vomiting, and abdominal pain. His laboratory findings were significant for lipase more than 10 000 on admission, and computed tomography scan of abdomen was showing peripancreatic fat stranding and inflammation. After exclusion of most common causes of pancreatitis, pravastatin was found probable culprit for his symptoms, which he started taking 2 weeks ago. We also reviewed the literature on statins-induced acute pancreatitis. With increased uses of statins, physician need to be vigilant to suspect statins as a culprit in cases of pancreatitis with unknown etiology. Prompt discontinuation of statins is required in these cases.

[63] *Olszewska-Parasiewicz J, Szarpak Ł, Rogula S et al.* **Statins in COVID-19 Therapy**. Life (Basel) 2021; 11.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34208435
ABSTRACT
Inhibitors of 3-hydroxy-3methylgultaryl-coenzyme A reductase (statins) are one of the main groups of drugs used in preventing and treating cardiovascular diseases worldwide. They are widely available, cheap, and well-tolerated. Based on statins' pleiotropic properties, including improvement of endothelial dysfunction, antioxidant properties, atherosclerotic plaque stabilization, and inhibition of inflammatory responses, it can be hypothesized that the use of statins, at least as an adjuvant in antiviral therapy, may be justified. All these effects might be especially beneficial in patients with COVID-19, suffering from endothelial dysfunction, microvascular and macrovascular thrombosis, and cytokine storm. Here, we review the recent data regarding the pathophysiology of SARS-CoV-2 activity in host cells, proposed COVID-19 therapy, the pleiotropic activity of statins, and statins in clinical trials in respiratory infections. According to the guidelines of the European and American Cardiac Societies, in patients with cardiovascular disease or high cardiovascular risk with concomitant COVID-19 it is recommended to continue statin treatment. However, the initiation of statin therapy de novo in COVID-19 treatment should only be done as part of a clinical trial.

[64] *Lee M, Ovbiagele B, Saver JL*. **Intensive Medical Management to Prevent Large and Small Artery Atherothrombotic Stroke: Time to Expand the Horizon**. Jama 2021; 326:217-218.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34196657
ABSTRACT

[65] *Koohi F, Khalili D, Mansournia MA et al.* **Multi-trajectories of lipid indices with incident cardiovascular disease, heart failure, and all-cause mortality: 23 years follow-up of two US cohort studies**. Journal of translational medicine 2021; 19:286.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34217318
ABSTRACT
BACKGROUND: Understanding the distinct patterns (trajectories) of variation in blood lipid levels before diagnosing cardiovascular disease (CVD) might carry important implications for improving disease prevention or treatment. METHODS: We investigated 14,373 participants (45.5% men) aged 45-84 from two large US prospective cohort studies with a median of 23 years follow-up. First, we jointly estimated developmental trajectories of lipid indices, including low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride (TG) concentrations using group-based multi-trajectory modeling. Then, the association of identified multi-trajectories with incident CVD, heart failure, and all-cause mortality were examined using Cox proportional hazard model. RESULTS: Seven distinct multi-trajectories were identified. The majority of participants (approximately 80%) exhibited decreasing LDL-C but rising TG levels and relatively stable HDL-C levels. Compared to the individuals with healthy and stable LDL-C, HDL-C, and TG levels, those in other groups were at significant risk of incident CVD after adjusting for other conventional risk factors. Individuals with the highest but decreasing LDL-C and borderline high and rising TG levels over time were at the highest risk than those in other groups with a 2.22-fold risk of CVD. Also, those with the highest and increased triglyceride levels over time, over optimal and decreasing LDL-C levels, and the lowest HDL-C profile had a nearly 1.84 times CVD risk. Even individuals in the multi-trajectory group with the highest HDL-C, optimal LDL-C, and optimal TG levels had a significant risk (HR, 1.45; 95% CI 1.02-2.08). Furthermore, only those with the highest HDL-C profile increased the risk of heart failure by 1.5-fold (95% CI 1.07-2.06). CONCLUSIONS: The trajectories and risk of CVD identified in this study demonstrated that despite a decline in LDL-C over time, a significant amount of residual risk for CVD remains. These findings suggest the impact of the increasing trend of TG on CVD risk and emphasize the importance of assessing the lipid levels at each visit and undertaking potential interventions that lower triglyceride concentrations to reduce the residual risk of CVD, even among those with the optimal LDL-C level.

[66] *Jurcau A, Simion A*. **Cognition, Statins, and Cholesterol in Elderly Ischemic Stroke Patients: A Neurologist's Perspective**. Medicina (Kaunas, Lithuania) 2021; 57.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34199243
ABSTRACT
Background and Objectives: The efficacy of hydroxy methyl glutaryl-coenzyme A reductase inhibitors (statins) in reducing the incidence of cardiovascular events pushed the target LDL-cholesterol (LDL-C) levels lower and lower in successive guidelines despite signals regarding potential cognitive side effects. We evaluated the relationship between cognitive impairment and LDL-C levels in elderly ischemic stroke patients. Materials and Methods: 29 ischemic stroke patients aged 65 and above with

LDL-C levels ≤70 mg/dL, classified according to the TOAST criteria, underwent detailed neuropsychological testing comprising the MMSE test, Montreal Cognitive Assessment (MoCA) and Addenbrooke's Cognitive Evaluation (ACE-III) test. Their performances were compared to those of 29 age-matched ischemic stroke patients with LDL-Cl levels >71 mg/dL. Results: The MMSE test failed to detect significant cognitive differences between the two groups. The MoCA and ACE-III tests detected impairments in visuo-spatial/executive function, attention, and recall/memory in patients with low LDL-C. A stepwise linear regression model of the ACE-III total scores revealed that LDL-cholesterol levels could contribute to 13.8% of the detected cognitive dysfunction, second in importance only to age, which contributed to 38.8% of the detected impairment. Conclusions: Physicians should be cautious when prescribing statins to elderly people. Hydrophilic ones may be preferred in cognitively impaired patients.

[67] *Htun KT, Pan J, Pasanta D et al.* **Identification of Metabolic Phenotypes in Young Adults with Obesity by (1)H NMR Metabolomics of Blood Serum**. Life (Basel) 2021; 11.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34207003

ABSTRACT

Since the obesity prevalence rate has been consistently increasing, it is necessary to find an effective way to prevent and treat it. Although progress is being made to reduce obesity in the young adult population, a better understanding of obesity-related metabolomics and related biochemical mechanisms is urgently needed for developing appropriate screening strategies. Therefore, the aim of this study is to identify the serum metabolic profile associated with young adult obesity and its metabolic phenotypes. (2) Methods: The serum metabolic profile of 30 obese and 30 normal-weight young adults was obtained using proton nuclear magnetic resonance spectroscopy ((1)H NMR). (1)H NMR spectra were integrated into 24 integration regions, which reflect relative metabolites, and were used as statistical variables. (3) Results: The obese group showed increased levels of lipids, glucose, glutamate, N-acetyl glycoprotein, alanine, lactate, 3 hydroxybutyrate and branch chain amino acid (BCAA), and decreased levels of choline as compared with the normal-weight group. Non-hyperlipidemia obese adults showed lower levels of lipids and lactate, glutamate, acetoacetate, N-acetyl glycoprotein, isoleucine, and higher levels of choline and glutamine, as compared with hyperlipidemic obese adults. (4) Conclusions: This study reveals valuable findings in the field of metabolomics and young adult obesity. We propose several serum biomarkers that distinguish between normal weight and obese adults, i.e., glutamine (higher in the normal group, $p < 0.05$), and lactate, BCAAs, acetoacetate and 3-hydroxybutyrate (higher in the obese group, $p < 0.05$). In addition, visceral fat and serum TG, glutamate, acetoacetate, N-acetyl glycoprotein, unsaturated lipid, isoleucine, and VLDL/LDL are higher ($p < 0.05$) in the obese with hyperlipidemia. Therefore, they can be used as biomarkers to identify these two types of obesity.

[68] *Hansen MW, Ørn S, Erevik CB et al.* **Regular consumption of cod liver oil is associated with reduced basal and exercise-induced C-reactive protein levels; a prospective observational trial : A NEEDED (The North Sea Race Endurance Exercise Study) 2014 sub-study**. Journal of the International Society of Sports Nutrition 2021; 18:51.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34183020

ABSTRACT

BACKGROUND: Dietary supplement use among recreational athletes is common, with the intention of reducing inflammation and improving recovery. We aimed to describe the relationship between omega-3 fatty acid supplement use and inflammation induced by strenuous exercise. METHODS: C-reactive protein (CRP) concentrations were measured in 1002 healthy recreational athletes before and 24 h after a 91-km bicycle race. The use of omega-3 fatty acid supplements was reported in 856 out of 1002 recreational athletes, and the association between supplement use and the exercise-induced CRP response was assessed. RESULTS: Two hundred seventy-four subjects reported regular use of omega-3 fatty acid supplements. One hundred seventy-three of these used cod liver oil (CLO). Regular users of omega-3 fatty acid supplements had significantly lower basal and exercise-induced CRP levels as compared to non-users ($n = 348$, $p < 0.001$). Compared to non-users, regular users had a 27% (95% confidence interval (CI): 14-40) reduction in Ln CRP response (unadjusted model, $p < 0.001$) and 16% (95% CI: 5-28, $p = 0.006$) reduction after adjusting for age, sex, race duration, body mass index, delta creatine kinase, MET hours per week, resting heart rate and higher education. CLO was the primary driver of this response with a 34% (95% CI: 19-49) reduction (unadjusted model, $p < 0.001$) compared to non-users. Corresponding numbers in the adjusted model were 24% (95% CI: 11-38, $p < 0.001$). CONCLUSION: Basal CRP levels were reduced, and the exercise-induced CRP response was attenuated in healthy recreational cyclists who used omega-3 fatty acid supplements regularly. This effect was only present in regular users of CLO. TRIAL REGISTRATION: NCT02166216 , registered June 18, 2014 - Retrospectively registered.

[69] *Zujko ME, Rożniata M, Zujko K*. **Individual Diet Modification Reduces the Metabolic Syndrome in Patients Before Pharmacological Treatment**. Nutrients 2021; 13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34205362

ABSTRACT

Modification of lifestyle, including healthy nutrition, is the primary approach for metabolic syndrome (MetS) therapy. The aim of this study was to estimate how individual nutrition intervention affects the reduction of MetS components. Subjects diagnosed with MetS were recruited in the Lomza Medical Centre. The study group consisted of 90 participants and was divided into one intervention group (individual nutrition education group (INEG)) and one control group (CG). The research was conducted over 3 months. The following measurements were obtained during the first visit and after completion of the 3 months intervention: body mass, waist circumference, body composition, blood pressure, fasting glucose, and blood lipids. Dietary assessments were performed before and post-intervention using 3-day 24-h dietary recalls. Dietary knowledge was evaluated with the KomPAN questionnaire. The total polyphenol content of the diet was calculated. Sociodemographic and lifestyle characteristics were collected from a self-reported questionnaire. The physical activity was assessed by the short version of the International Physical Activity Questionnaire (IPAQ). It was found that the individual nutrition education was an effective method to improve the knowledge, dietary habits, and physical activity of the study participants. The modification of the diet in terms of higher intake of polyphenols (flavonoids and anthocyanins), fiber, polyunsaturated fatty acids (PUFA), PUFA n-3, and lower intake of saturated fatty acids (SFA) had a significant impact on the improvement of some MetS risk factors (waist circumference, fasting glucose, and HDL-cholesterol).

[70] *Vergara M, Hauser ME, Aronica L et al.* **Associations of Changes in Blood Lipid Concentrations with Changes in Dietary Cholesterol Intake in the Context of a Healthy Low-**

Carbohydrate Weight Loss Diet: A Secondary Analysis of the DIETFITS Trial. Nutrients 2021; 13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34200027
ABSTRACT
In 2015, the Dietary Guidelines for Americans (DGA) eliminated the historical upper limit of 300 mg of dietary cholesterol/day and shifted to a more general recommendation that cholesterol intake should be limited. The primary aim of this secondary analysis of the Diet Intervention Examining the Factors Interacting With Treatment Success (DIETFITS) weight loss diet trial was to evaluate the associations between 12-month changes in dietary cholesterol intake (mg/day) and changes in plasma lipids, particularly low-density lipoprotein (LDL) cholesterol for those following a healthy low-carbohydrate (HLC) diet. Secondary aims included examining high-density lipoprotein (HDL) cholesterol and triglycerides and changes in refined grains and added sugars. The DIETFITS trial randomized 609 healthy adults aged 18-50 years with body mass indices of 28-40 kg/m(2) to an HLC or healthy low-fat (HLF) diet for 12 months. Linear regressions examined the association between 12-month change in dietary cholesterol intake and plasma lipids in 208 HLC participants with complete diet and lipid data, adjusting for potential confounding variables. Baseline dietary cholesterol intake was 322 ± 173 (mean ± SD). At 12 months, participants consumed an average of 460 ± 227 mg/day of dietary cholesterol; 76% consumed over the previously recommended limit of 300 mg/day. Twelve-month changes in cholesterol intake were not significantly associated with 12-month changes in LDL-C, HDL-C, or triglycerides. Diet recall data suggested participants' increase in dietary cholesterol was partly due to replacing refined grains and sugars with eggs. An increase in daily dietary cholesterol intake to levels substantially above the previous 300 mg upper limit was not associated with a negative impact on lipid profiles in the setting of a healthy, low-carbohydrate weight loss diet.

[71] *Su X, Cheng Y, Zhang G, Wang B*. **Novel insights into the pathological mechanisms of metabolic related dyslipidemia**. Molecular biology reports 2021; 48:5675-5687.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34218408
ABSTRACT
Due to the technological advances, it has been well-established that obesity is strongly correlated with various health problems. Among these problems, dyslipidemia is one of the most important concomitant symptoms under obese status which is the main driving force behind the pathological progression of cardio-metabolic disorder diseases. Importantly, the type of dyslipidemia, arising from concerted action of obesity, has been identified as "metabolic related dyslipidemia", which is characterized by increased circulating levels of Low density lipoprotein cholesterol (LDL-C), Triglycerides (TG) accompanied by lower circulating levels of High density lipoprotein cholesterol (HDL-C). On the other hand, the metabolic related dyslipidemia is being verified as a vital link between obesity and hypertension, diabetes mellitus, and Cardiovascular disease (CVD). In this review, we summarized the current understanding of metabolic related dyslipidemia and the potential mechanisms which lead to the pathogenesis of obesity. Meanwhile, we also summarized the emerging results which focused on several novel lipid bio-markers in metabolic related dyslipidemia, such as pro-protein convertase subtilisin/kexin type 9 (PCSK9) and sphingosine-1-phosphate (S1P), and their potential use as biomarkers of metabolic related dyslipidemia.

[72] *Rajalahti T, Aadland E, Resaland GK et al.* **Cardiometabolic Associations between Physical Activity, Adiposity, and Lipoprotein Subclasses in Prepubertal Norwegian Children**. Nutrients 2021; 13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34205279
ABSTRACT
Lipoprotein subclasses possess crucial cardiometabolic information. Due to strong multicollinearity among variables, little is known about the strength of influence of physical activity (PA) and adiposity upon this cardiometabolic pattern. Using a novel approach to adjust for covariates, we aimed at determining the "net" patterns and strength for PA and adiposity to the lipoprotein profile. Principal component and multivariate pattern analysis were used for the analysis of 841 prepubertal children characterized by 26 lipoprotein features determined by proton nuclear magnetic resonance spectroscopy, a high-resolution PA descriptor derived from accelerometry, and three adiposity measures: body mass index, waist circumference to height, and skinfold thickness. Our approach focuses on revealing and validating the underlying predictive association patterns in the metabolic, anthropologic, and PA data to acknowledge the inherent multicollinear nature of such data. PA associates to a favorable cardiometabolic pattern of increased high-density lipoproteins (HDL), very large and large HDL particles, and large size of HDL particles, and decreasedtriglyceride, chylomicrons, very low-density lipoproteins (VLDL), and their subclasses, and to low size of VLDL particles. Although weakened in strength, this pattern resists adjustment for adiposity. Adiposity is inversely associated to this pattern and exhibits unfavorable associations to low-density lipoprotein (LDL) features, including atherogenic small and very small LDL particles. The observed associations are still strong after adjustment for PA. Thus, lipoproteins explain 26.0% in adiposity after adjustment for PA compared to 2.3% in PA after adjustment for adiposity.

[73] *Pajkowski M, Dudziak M, Chlebus K, Hellmann M.* **Assessment of microvascular function and pharmacological regulation in genetically confirmed familial hypercholesterolemia**. Microvascular research 2021; 138:104216.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34182004
ABSTRACT
BACKGROUND: Familial hypercholesterolemia (FH) is a genetic lipid disorder leading to accelerated atherosclerosis, premature cardiovascular disease and death. Microvascular endothelial dysfunction is one of the earliest vascular pathology manifestations and may precede symptomatic atherosclerosis. METHODS: In this paper, microvascular endothelial function was assessed in FH patients and healthy controls using flow mediated skin fluorescence (FMSF), based on measurements of nicotinamide adenine dinucleotide fluorescence intensity during brachial artery occlusion (ischemic response, IR) and immediately after occlusion (hyperemic response, HR). Low-density lipoprotein cholesterol (LDL-C) and total cholesterol (TC) were used to assess its relation with microvascular parameters evaluated in vivo. RESULTS: LDL-C levels were significantly correlated to both HR(max) ($r = -0.548$, $p = 0.001$) and HR(index) ($r = -0.514$, $p = 0.003$). Similarly, there was a significant inverse correlation of TC levels and both HR(max) ($r = -0.538$, $p = 0.002$) and HR(index) ($r = -0.512$, $p = 0.003$). All FMSF parameters were found lower in FH patients compared to age- and sex-matched healthy controls. Hyperemic response (HR(max)) was significantly higher in FH patients examined on statins compared to those without any lipid-lowering treatment (19.9 ± 3.1 vs. 16.4 ± 4.2 respectively, $p = 0.022$). CONCLUSIONS: This study shows that, in patients with FH, microvascular

endothelial-dependent hyperemic response is impaired and inversely correlated to plasma cholesterol levels. Microvascular function was found better in FH patients receiving statins.

[74] *Natale F, Capasso R, Casalino A et al.* **Peripheral Artery Disease and Abdominal Aortic Aneurysm: The Forgotten Diseases in COVID-19 Pandemic. Results from an Observational Study on Real-World Management**. Medicina (Kaunas, Lithuania) 2021; 57.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34209552

ABSTRACT

Background and Objectives: It is well established that patients with peripheral artery disease (PAD) as well abdominal aortic aneurysm (AAA) have an increased cardiovascular (CV) mortality. Despite this higher risk, PAD and AAA patients are often suboptimality treated. This study assessed the CV profile of PAD and AAA patients, quantifying the survival benefits of target-based risk-factors modification even in light of the COVID-19 pandemic. Materials and Methods: PAD and AAA patients admitted for any reason to the Vascular Unit from January 2019 to February 2020 were retrospectively analyzed. Biochemical and CV profiles as well as ongoing medical therapies were recorded. Benefits of CV risk-factors control were estimated using the SMART-REACH model. A follow-up visit during the year 2020 was scheduled. Results: A total of 669 patients were included. Of these, 190 showed AAA and 479 PAD at any stage. Only 54% of PAD and 41% of AAA patients were on lipid-lowering drugs with non-optimal low-density lipoprotein (LDL) levels for most of them. A better control of all modifiable CV risk-factors based on the current guidelines would offer an absolute risk reduction of the mean 10-year CV risk by 9% in PAD and 14% in AAA. Unfortunately, the follow-up visit was lost because of COVID-19 limitations. Conclusions: Lipid profiles of PAD and AAA patients were far from guideline-based targets, and medical management was suboptimal. In our center, the COVID-19 pandemic impacted on the strict surveillance required in these very high-risk patients. The achievement of guideline-based therapeutic targets would definitively confer additional significant benefits in reducing the CV risk in these patients.

[75] *Moliterno P, Donangelo CM, Borgarello L et al.* **Association of Dietary Patterns with Cardiovascular and Kidney Phenotypes in an Uruguayan Population Cohort**. Nutrients 2021; 13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34199124

ABSTRACT

The impact of habitual diet on chronic diseases has not been extensively characterized in South America. We aimed to identify major dietary patterns (DP) in an adult cohort in Uruguay (Genotype Phenotype and Environment of Hypertension Study-GEFA-HT-UY) and to assess associations with metabolic, anthropometric characteristics, and cardiovascular and kidney phenotypes. In a cross-sectional study (n = 294), DP were derived by the principal component analysis. Blood and urine parameters, anthropometrics, blood pressure, pulse wave velocity, and glomerular filtration rate were measured. Multivariable adjusted linear models and adjusted binary logistic regression were used. Three DP were identified (Meat, Prudent, Cereal and Mate) explaining 22.6% of total variance in food intake. The traditional Meat DP, characterized by red and barbecued meat, processed meat, bread, and soft drinks, was associated with worse blood lipid profile. Prudent DP, characterized by vegetables, fish, and nuts, and lower loads for bread and crackers, was associated with reduced risk of vitamin D deficiency. Cereal and Mate DP, was characterized by higher loads of cereals, bread, and crackers, and mate infusion, with higher odds of excessive body weight. No direct associations of

dietary patterns with hypertension, arterial stiffness, chronic kidney disease, and nephrolithiasis were found in the studied population, nor by age categories or sex.

[76] *Johansson A, Drake I, Engström G, Acosta S*. **Modifiable and Non-Modifiable Risk Factors for Atherothrombotic Ischemic Stroke among Subjects in the Malmö Diet and Cancer Study**. Nutrients 2021; 13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34204127

ABSTRACT

Risk factors for ischemic stroke is suggested to differ by etiologic subtypes. The purpose of this study was to examine the associations between modifiable and non-modifiable risk factors and atherothrombotic stroke (i.e., excluding cardioembolic stroke), and to examine if the potential benefit of modifiable lifestyle factors differs among subjects with and without predisposing comorbidities. After a median follow-up of 21.2 years, 2339 individuals were diagnosed with atherothrombotic stroke out of 26,547 study participants from the Malmö Diet and Cancer study. Using multivariable Cox regression, we examined non-modifiable (demographics and family history of stroke), semi-modifiable comorbidities (hypertension, dyslipidemia, diabetes mellitus and atherosclerotic disease), and modifiable (smoking, body mass index, diet quality, physical activity, and alcohol intake) risk factors in relation to atherothrombotic stroke. Higher age, male gender, family history of stroke, and low educational level increased the risk of atherothrombotic stroke as did predisposing comorbidities. Non-smoking (hazard ratio (HR) = 0.62, 95% confidence interval (CI) 0.56-0.68), high diet quality (HR = 0.83, 95% CI 0.72-0.97) and high leisure-time physical activity (HR = 0.89, 95% CI 0.80-0.98) decreased the risk of atherothrombotic ischemic stroke independent of established risk factors, with non-significant associations with body mass index and alcohol intake. The effect of the lifestyle factors was independent of predisposing comorbidities at baseline. The adverse effects of several cardiovascular risk factors were confirmed in this study of atherothrombotic stroke. Smoking cessation, improving diet quality and increasing physical activity level is likely to lower risk of atherothrombotic stroke in the general population as well as in patient groups at high risk.

[77] *Dimache AM, Șalaru DL, Sascău R, Stătescu C*. **The Role of High Triglycerides Level in Predicting Cognitive Impairment: A Review of Current Evidence**. Nutrients 2021; 13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34203094

ABSTRACT

The burden of cognitive disorders is huge and still growing, however the etiology and the degree of cognitive impairment vary considerably. Neurodegenerative and vascular mechanisms were most frequently assessed in patients with dementia. Recent studies have shown the possible involvement of triglycerides levels in cognitive function through putative mechanisms such as brain blood barrier dysfunction or amyloid metabolism imbalance, but not all research in the field found this association. Several clinical studies evaluated the relationship between different forms of cognitive decline and levels of serum triglycerides, independent of other cardiovascular risk factors. This review focuses on the role of triglycerides in cognitive decline, cerebral amyloidosis and vascular impairment. Considering that the management of hypertriglyceridemia benefits from lifestyle modification, diet, and specific drug therapy, future studies are requested to appraise the triglycerides-cognitive impairment relationship.

[78] *Costabile G, Della Pepa G, Vetrani C et al.* **An Oily Fish Diet Improves Subclinical Inflammation in People at High Cardiovascular Risk: A Randomized Controlled Study**. Molecules (Basel, Switzerland) 2021; 26.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34199645

ABSTRACT

Interest has arisen on the anti-inflammatory action of dietary components, including long-chain n-3 fatty acids (LCn3) and polyphenols (PP). The aim of this study was to evaluate the effects of diets rich in PP and oily fish (high-LCn3 diets) on markers of subclinical inflammation and growth factors in people at high cardiometabolic risk. Individuals with high waist circumference and one more component of metabolic syndrome were randomized to one of the following isoenergetic diets: low LCn3&PP, high LCn3, high PP, high LCn3&PP. Before and after 8 weeks, fasting and postprandial plasma concentrations of hs-CRP and fasting serum concentrations of IL-1, IL-4, IL-6, IL-10, IL-17, INF-, TNF-, FGF, VEGF, PDGF-, G-CSF, and GM-CSF were determined. An oily fish diet reduced fasting plasma hs-CRP (1.28 ± 12.0, -12.5 ± 6.9, 22.5 ± 33.6, -12.2 ± 11.9; 8-week percent change, Mean ± SEM; low LCn3&PP, high LCn3, high PP, high LCn3&PP group, respectively), postprandial 6h-AUC hs-CRP (4.6 ± 16.3, -18.2 ± 7.2, 26.9 ± 35.1, -11.5 ± 11.8, 8-week percent change) and fasting IL-6 (20.8 ± 18.7, -2.44 ± 12.4, 28.1 ± 17.4, -9.6 ± 10.2), IL-17 (2.40 ± 4.9, -13.3 ± 4.9, 3.8 ± 4.43, -11.5 ± 4.7), and VEGF (-5.7 ± 5.8, -5.6 ± 7.5, 3.5 ± 5.8, -11.1 ± 5.5) (8-week percent change; $p < 0.05$ for LCn3 effect for all; no significant effect for PP; 2-factor ANOVA). An oily fish diet improved subclinical inflammation, while no significant effect was observed for dietary polyphenols.

[79] *Whiteley WN, Gupta AK, Godec T et al.* **Long-Term Incidence of Stroke and Dementia in ASCOT**. Stroke 2021:Strokeaha120033489.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34192893

ABSTRACT

BACKGROUND AND PURPOSE: Management of stroke risk factors might reduce later dementia. In ASCOT (Anglo-Scandinavian Outcome Trial), we determined whether dementia or stroke were associated with different blood pressure (BP)-lowering regimens; atorvastatin or placebo; and mean BP, BP variability, and mean cholesterol levels. METHODS: Participants with hypertension and ≥3 cardiovascular disease risk factors were randomly allocated to amlodipine- or atenolol-based BP-lowering regimen targeting BP <140/90 mm Hg for 5.5 years. Participants with total cholesterol ≤6.5 mmol/L were also randomly allocated to atorvastatin 10 mg or placebo for 3.3 years. Mean and LDL (low-density lipoprotein) cholesterol, BP, and SD of BP were calculated from 6 months to end of trial. UK participants were linked to electronic health records to ascertain deaths and hospitalization in general and mental health hospitals. Dementia and stroke were ascertained by validated code lists and within-trial ascertainment. RESULTS: Of 8580 UK participants, 7300 were followed up to 21 years from randomization. Atorvastatin for 3.3 years had no measurable effect on stroke (264 versus 272; adjusted hazard ratio [HR], 0.92 [95% CI, 0.78-1.09]; P=0.341) or dementia (238 versus 227; adjusted HR, 0.98 [95% CI, 0.82-1.18]; P=0.837) compared with placebo. Mean total cholesterol was not associated with later stroke or dementia. An amlodipine-based compared with an atenolol-based regimen for 5.5 years reduced stroke (443 versus 522; adjusted HR, 0.82 [95% CI, 0.72-0.93]; P=0.003) but not dementia (450 versus 465; adjusted HR, 0.94 [95% CI, 0.82-1.07]; P=0.334) over follow-up. BP variability (SD mean BP) was associated with a higher risk of dementia (per 5 mm Hg HR, 1.14 [95% CI, 1.06-1.24]; P<0.001) and stroke (HR, 1.21 [95% CI, 1.12-1.32]; P<0.001) adjusted

for mean BP. CONCLUSIONS: An amlodipine-based BP regimen reduced the long-term incidence of stroke compared with an atenolol-based regimen but had no measurable effect on dementia. Atorvastatin had no effect on either stroke or dementia. Higher BP variability was associated with a higher incidence of later dementia and stroke.

[80] *Ruscica M, Penson PE, Ferri N et al.* **Impact of nutraceuticals on markers of systemic inflammation: Potential relevance to cardiovascular diseases - A position paper from the International Lipid Expert Panel (ILEP)**. Prog Cardiovasc Dis 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34186099
ABSTRACT
Inflammation is a marker of arterial disease stemming from cholesterol-dependent to -independent molecular mechanisms. In recent years, the role of inflammation in atherogenesis has been underpinned by pharmacological approaches targeting systemic inflammation that have led to a significant reduction in cardiovascular disease (CVD) risk. Although the use of nutraceuticals to prevent CVD has largely focused on lipid-lowering (e.g, red-yeast rice and omega-3 fatty acids), there is growing interest and need, especially now in the time of coronavirus pandemic, in the use of nutraceuticals to reduce inflammatory markers, and potentially the inflammatory CVD burden, however, there is still not enough evidence to confirm this. Indeed, diet is an important lifestyle determinant of health and can influence both systemic and vascular inflammation, to varying extents, according to the individual nutraceutical constituents. Thus, the aim of this Position Paper is to provide the first attempt at recommendations on the use of nutraceuticals with effective anti-inflammatory properties.

[81] *Ravnskov U.* **Is High Cholesterol Deleterious? An Alternative Point of View. Comment on Burén et al. A Ketogenic Low-Carbohydrate High-Fat Diet Increases LDL Cholesterol in Healthy, Young, Normal-Weight Women: A Randomized Controlled Feeding Trial. Nutrients 2021, 13, 814**. Nutrients 2021; 13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34205486
ABSTRACT
In their study of the effect of an LCHF-diet on blood lipids, Burén et al. [...].

[82] *Otrante A, Trigui A, Walha R et al.* **Extra Virgin Olive Oil Prevents the Age-Related Shifts of the Distribution of HDL Subclasses and Improves Their Functionality**. Nutrients 2021; 13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34209930
ABSTRACT
High-density lipoproteins (HDL) maintain cholesterol homeostasis through the role they play in regulating reverse cholesterol transport (RCT), a process by which excess cholesterol is transported back to the liver for elimination. However, RCT can be altered in the presence of cardiovascular risk factors, such as aging, which contributes to the increase in the incidence of cardiovascular diseases (CVD). The present study was aimed at investigating the effect of extra virgin olive oil (EVOO) intake on the cholesterol efflux capacity (CEC) of HDL, and to elucidate on the mechanisms by which EVOO intake improves the anti-atherogenic activity of HDL. A total of 84 healthy women and men were enrolled and were distributed, according to age, into two groups: 27 young (31.81 ± 6.79 years) and 57 elderly (70.72 ± 5.6 years) subjects. The subjects in both groups were given 25 mL/d of extra

virgin olive oil (EVOO) for 12 weeks. CEC was measured using J774 macrophages radiolabeled with tritiated cholesterol (((3)H) cholesterol). HDL subclass distributions were analyzed using the Quantimetrix Lipoprint® system. The HDL from the elderly subjects exhibited a lower level of CEC, at 11.12% ($p < 0.0001$), than the HDL from the young subjects. The CEC of the elderly subjects returned to normal levels following 12 weeks of EVOO intake. An analysis of the distribution of HDL subclasses showed that HDL from the elderly subjects were composed of lower levels of large HDL (L-HDL) ($p < 0.03$) and higher levels of small HDL (S-HDL) ($p < 0.002$) compared to HDL from the young subjects. A multiple linear regression analysis revealed a positive correlation between CEC and L-HDL levels ($r = 0.35$ and $p < 0.001$) as well as an inverse correlation between CEC and S-HDL levels ($r = -0.27$ and $p < 0.01$). This correlation remained significant even when several variables, including age, sex, and BMI as well as low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and glucose levels ($\beta = 0.28$, $p < 0.002$, and $\beta = 0.24$, $p = 0.01$) were accounted for. Consuming EVOO for 12 weeks modulated the age-related difference in the distribution of HDL subclasses by reducing the level of S-HDL and increasing the level of intermediate-HDL/large-HDL (I-HDL/L-HDL) in the elderly subjects. The age-related alteration of the CEC of HDL was due, in part, to an alteration in the distribution of HDL subclasses. A diet enriched in EVOO improved the functionality of HDL through an increase in I-HDL/L-HDL and a decrease in S-HDL.

[83] *Muñoz-Perez DM, Gonzalez-Correa CH, Astudillo-Muñoz EY et al.* **Alternative Foods in Cardio-Healthy Dietary Models That Improve Postprandial Lipemia and Insulinemia in Obese People**. Nutrients 2021; 13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34209561
ABSTRACT
Obesity is one of the major health problems worldwide. Following healthy dietary patterns can be difficult in some countries due to the lack of availability of certain foods; thus, alternative foods are needed. Our aim was to evaluate the effect of a dietary pattern consisting of fruit, avocado, whole grains, and trout (FAWGT) on postprandial insulinemia and lipemia in obese Colombian subjects. A randomized controlled crossover study was conducted, in which 44 subjects with BMI ≥ 30 kg/m(2) followed either a FAWGT diet or a diet high in saturated fat and rich in processed carbohydrates. Levels of lipids and carbohydrates were measured during the postprandial state. The FAWGT diet reduced fasting insulin, VLDL, and HOMA-IR after 8 weeks ($p < 0.05$), while there was a lower postprandial increase in TG, VLDL, and insulin levels after both acute and chronic intake of FAWGT diet ($p < 0.05$). The intake of FAWGT-diet was characterized by high consumption of foods rich in fiber, MUFAs, and vitamins C and E ($p < 0.05$). The consumption of a diet composed of fruit, avocado, whole grains, and trout has emerged as a valid alternative to the foods included in other heart-healthy diets since it improves postprandial lipemia and insulinemia in obese people and has similar beneficial effects to these healthy models.

[84] *Lunova T, Levytska L, Kucher S et al.* **Observation of serious adverse cardiovascular events over 3 years in patients with advanced atherosclerosis: is there a gender difference?** Polski merkuriusz lekarski : organ Polskiego Towarzystwa Lekarskiego 2021; 49:171-175.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34218233
ABSTRACT

Dyslipidemia has been widely acknowledged as one of the major predisposing factors for the development and progression of atherosclerosis. While advanced atherosclerosis confirmed to influence the prognosis of patients with acute coronary syndrome (ACS), it has not yet been established, whether this impact is gender-dependent. AIM: The aim of study was to investigate possible gender-related effect of dyslipidemia and generalized atherosclerosis on the long-term outcomes in patients with ACS. MATERIALS AND METHODS: A total of 247 patients (88 women and 159 men) with ACS were included. Sample was divided into two groups, according to gender. Patients' lipid and comorbidity profiles were assessed. Cumulative major adverse coronary events (MACE) were estimated throughout 3-year follow-up period. RESULTS: Women were older and had more comorbidities. Cumulative 3-year MACE rates were higher in women than in men (33% vs. 23%, p=0.06). In the multivariable Cox regression analysis abnormal lipid profiles were more significantly associated with higher MACE in females (HR=1.5, 95% CI [1-2,28], p<0.00001), compared with males (HR=1.0, 95% CI [0.5-2.08], p=0.4), as well as prior MI: (HR=3.8, 95% CI [1.4-10.5], p<0.00001) vs. (HR=1.9, 95% [0.8-4.2], p=0.009) and concomitant peripheral artery disease (PAD): (HR=5.2, 95% CI [1.5-18.2], p<0.00001) vs. (HR=2.2, 95% CI [0.73-6.6], p=0.02) respectively. CONCLUSIONS: In our study dyslipidemia, concomitant PAD and history of MI were independent predictors of higher MACE more significantly in females with ACS than in males. Thus, it can be assumed that female patients require an increased medical attention with strict serum lipid control.

[85] *Guo Q, Tang Y, Li Y et al.* **Perinatal High-Salt Diet Induces Gut Microbiota Dysbiosis, Bile Acid Homeostasis Disbalance, and NAFLD in Weanling Mice Offspring**. Nutrients 2021; 13. **PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34206629

ABSTRACT

A perinatal high-salt (HS) diet was reported to elevate plasma triglycerides. This study aimed to investigate the hypothesis that a perinatal HS diet predisposed offspring to non-alcoholic fatty liver disease (NAFLD), the hepatic manifestation of abnormal lipid metabolism, and the possible mechanism. Female C57BL/6 mice were fed a control diet (0.5% NaCl) or HS diet (4% NaCl) during pregnancy and lactation and their offspring were sacrificed at weaning. The perinatal HS diet induced greater variation in fecal microbial beta-diversity (β-diversity) and increased bacteria abundance of Proteobacteria and Bacteroides. The gut microbiota dysbiosis promoted bile acid homeostasis disbalance, characterized by the accumulation of lithocholic acid (LCA) and deoxycholic acid (DCA) in feces. These alterations disturbed gut barrier by increasing the expression of tight junction protein (Tjp) and occludin (Ocln), and increased systemic lipopolysaccharide (LPS) levels and hepatic inflammatory cytokine secretion (TNF-α and IL-6) in the liver. The perinatal HS diet also inhibited hepatic expression of hepatic FXR signaling (CYP7A1 and FXR), thus triggering increased hepatic expression of pro-inflammatory cytokines (TNF-α and IL-6) and hepatic lipid metabolism-associated genes (SREBP-1c, FAS, ACC), leading to unique characteristics of NAFLD. In conclusion, a perinatal HS diet induced NAFLD in weanling mice offspring; the possible mechanism was related to increased bacteria abundance of Proteobacteria and Bacteroides, increased levels of LCA and DCA in feces, and increased expressions of hepatic FXR signaling.

[86] *Burén J, Ericsson M, Damasceno NRT, Sjödin A*. **Reply to Ravnskov, U. Is High Cholesterol Deleterious? An Alternative Point of View. Comment on "Burén et al. A Ketogenic Low-**

Carbohydrate High-Fat Diet Increases LDL Cholesterol in Healthy, Young, Normal-Weight Women: A Randomized Controlled Feeding Trial. Nutrients 2021, 13, 814". Nutrients 2021; 13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34206157
ABSTRACT
We thank Ravnskov [...].

[87] *Bordbar M, de Mutsert R, Cevval M et al.* **Differential effect of statin use on coagulation markers: an active comparative analysis in the NEO study**. Thromb J 2021; 19:45.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34176487
ABSTRACT
BACKGROUND: Statins are a potential treatment for venous thromboembolism (VTE) prophylaxis complementary to conventional anticoagulants without associated bleeding complications. This study aimed to compare pro-thrombotic activities of different classes of lipid-lowering drugs in an active comparator design and determine whether there is a relation between statin versus fibrate/niacin use and pro-coagulant factor outcomes. METHODS: This is a cross-sectional analysis of participants from the Netherlands Epidemiology of Obesity study using any class of lipid-lowering drugs, including any types of statins, niacin, and fibrates. We performed linear regression analyses to determine fibrinogen, factor (F) VIII, FIX, and FXI activity in statins versus fibrate/niacin users and adjusted for age, sex, tobacco smoking, body mass index (BMI), hypertension, diabetes, and prevalent cardiovascular disease. RESULTS: Among 1043 participants, the mean age was 58.4 ± 5.2 years, 61% were men, and the mean BMI was 31.3 ± 4.5 kg/m(2). Clinical characteristics were balanced between statin and fibrate/niacin users. Statin users had lower mean FXI (18.3 IU/dL, 95% confidence interval (CI) 9.4 to 27.3) levels compared to fibrate/niacin users. The level of FVIII (15.8 IU/dL, 95% CI -0.003 to 31.6), and FIX (11.3 IU/dL, 95% CI -0.4 to 23.2) were lower in statin users than fibrate/niacin users with marginal statistical significance. CONCLUSION: Current statin use was associated with lower plasma levels of FXI than fibrate/niacin use. The effects on coagulation factors may, in part, explain the benefit of statin therapy rendered in primary and secondary prevention of VTE.

[88] *Aleksova A, Gagno G, Pierri A et al.* **What the Cardiologist Needs to Consider in the Management of Oncologic Patients with STEMI-Like Syndrome: A Case Report and Literature Review**. Pharmaceuticals (Basel, Switzerland) 2021; 14.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34204714
ABSTRACT
In pre-hospital care, an accurate and quick diagnosis of ST-segment elevation myocardial infarction (STEMI) is imperative to promptly kick-off the STEMI network with a direct transfer to the cardiac catheterization laboratory (cath lab) in order to reduce myocardial infarction size and mortality. Aa atherosclerotic plaque rupture is the main mechanism responsible for STEMI. However, in a small percentage of patients, emergency coronarography does not reveal any significant coronary stenosis. The fluoropyrimidine agents such as 5-Fluorouracil (5-FU) and capecitabine, widely used to treat gastrointestinal, breast, head and neck cancers, either as a single agent or in combination with other chemotherapies, can cause potentially lethal cardiac side effects. Here, we present the case of a patient with 5-FU cardiotoxicity resulting in an acute coronary syndrome (ACS) with recurrent episodes of chest pain and ST-segment elevation.. Our case report highlights the importance of

widening the knowledge among cardiologists of the side effects of chemotherapeutic drugs, especially considering the rising number of cancer patients around the world and that fluoropyrimidines are the main treatment for many types of cancer, both in adjuvant and advanced settings.