[1] *Chełstowska B, Barańczyk-Kuźma A, Kuźma-Kozakiewicz M*. **Dyslipidemia in patients with amyotrophic lateral sclerosis - a case control retrospective study**. Amyotrophic lateral sclerosis & frontotemporal degeneration 2020:1-11.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33103950

ABSTRACT

Amyotrophic lateral sclerosis (ALS) is a fatal, neurodegenerative disorder leading to quadriplegia and aphagia. While swallowing difficulties and increased energy demand lead to malnutrition, increased lipid concentration may correlate with survival and respiratory functions. Objective: To analyze the frequency and type of dyslipidemias in a large population of clinically characterized ALS patients (PALS). Methods: The retrospective study included clinical and laboratory data of 650 consecutive PALS fulfilling the El Escorial criteria and 365 age- and gender-matched hospital controls. Results: 65% of PALS suffered from dyslipidemia independently of concomitant metabolic diseases. The most frequent lipid disorder was hypercholesterolemia (35% PALS, 25% controls), followed by mixed dyslipidemia (24.6%, 14%), with rare cases of hypertriglyceridemia and atherogenic dyslipidemia. Triacylglycerols (TAG) and LDL/HDL correlated with BMI, while LDL/HDL and total cholesterol (TCh) with disease duration. Among PALS with concomitant metabolic diseases, TCh correlated with disease duration and ALSFRS-R, while TAG with respiratory functions (FVC) in patients without metabolic diseases. The highest median concentration of TCh, LDL and LDL/HDL was found in classic ALS and PMA and the lowest in PBP. Conclusion: Dyslipidemia occurs more frequently in PALS compared to controls and independently of concomitant metabolic diseases. Similar to the general population, the most frequent lipid disturbance is hypercholesterolemia, followed by mixed dyslipidemia. Although particular lipid parameters correlate with BMI and disease duration, they do not show strong correlations with disease progression rate. There is a need of randomized control trials assessing the risk and benefits of the use of lipid lowering agents in ALS.

[2] *Ateş AH, Yorgun H, Canpolat U et al.* **Long-Term Prognostic Value of Coronary Atherosclerotic Plaque Characteristics Assessed by Computerized Tomographic Angiography**. Angiology 2020:3319720963677.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33118364

ABSTRACT

We aimed to present the long-term prognostic role of coronary computed tomography angiography (CTA) in a cohort of patients with coronary artery disease (CAD) and noncritical stenosis. A total of 1138 patients who underwent coronary CTA for suspected CAD were included in the study. For the categorization of the coronary atherosclerotic plaque (CAP), the coronary system was divided into 16 segments. For each segment, CAPs were categorized as calcified, noncalcified, and mixed. All-cause and cardiovascular (CV) mortality data were collected for prognostic evaluation. Coronary CTA analyses showed that 34.5% of patients had noncalcified CAP, 14.5% of patients had calcified CAP, and 11% of patients had mixed CAP. During a median of 141.5 months follow-up, CV and all-cause mortality was observed in 57 (5%) and 149 (13.1%) patients, respectively. In multivariable Cox regression analysis, calcified CAP morphology and the extent of involved segments were significant predictors of both CV and all-cause mortality. The presence of calcified CAP morphology and the higher number of diseased coronary segments via coronary CTA might help stratify patients at risk for adverse

CV outcomes during long-term follow-up. Patients with these features at index coronary CTA may be evaluated more closely with aggressive preventive measures.

[3] *Chu T, Huang M, Zhao Z et al.* **Atorvastatin Reduces Accumulation of Vascular Smooth Muscle Cells to Inhibit Intimal Hyperplasia via p38 MAPK Pathway Inhibition in a Rat Model of Vein Graft**. Arquivos brasileiros de cardiologia 2020; 115:630-636.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33111860
ABSTRACT
BACKGROUND: The rate of saphenous vein graft failure one year after coronary artery bypass grafting ranges from 10% to 25%. The aim of this study was to explore whether atorvastatin can reduce accumulation of vascular smooth muscle cells to inhibit intimal hyperplasia via p38 MAPK pathway inhibition. METHODS: Forty-five Sprague-Dawley rats were randomized to three groups. Thirty rats received a vein graft operation, and they were randomized to be treated with vehicle or atorvastatin; fifteen rats received a sham operation. We detected intimal hyperplasia by hematoxylin-eosin staining and related protein expression by immunohistochemical and Western blot analysis. Comparisons were analyzed by single-factor analysis of variance and Fisher's least significant difference test, with $p < 0.05$ considered significant. RESULTS: The intima analyzed by hematoxylin-eosin staining was dramatically thicker in the control group than in the atorvastatin group and sham group ($p < 0.01$). The outcomes of immunohistochemical staining of α-SMA demonstrated that the percentage of α-SMA-positive cells in the control group was higher than in the atorvastatin group ($p < 0.01$). We also evaluated α-SMA, PCNA, p38 MAPK, and phosphorylation of p38 MAPK after statin treatment by Western blot analysis, and the results indicated that atorvastatin did not lead to p38 MAPK reduction ($p < 0.05$); it did, however, result in inhibition of p38 MAPK phosphorylation ($p < 0.01$), and it significantly reduced α-SMA and PCNA levels, in comparison with the control group ($p < 0.01$). CONCLUSION: We have demonstrated that atorvastatin can inhibit accumulation of vascular smooth muscle cells by inhibiting the p38 MAPK pathway, and it is capable of inhibiting intimal hyperplasia in a rat vein graft model.

[4] *Gatto M, Pagan LU, Mota GAF*. **Influence of Atorvastatin on Intimal Hyperplasia in the Experimental Model**. Arquivos brasileiros de cardiologia 2020; 115:637-638.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33111861
ABSTRACT

[5] *Blond K, Aarestrup J, Vistisen D et al.* **Associations between body mass index trajectories in childhood and cardiovascular risk factors in adulthood**. Atherosclerosis 2020; 314:10-17.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33129081
ABSTRACT
BACKGROUND AND AIMS: Children with a growth trajectory of overweight have higher levels of cardiovascular disease (CVD) risk factors than children with a normal-weight trajectory. However, less is known about how trajectories of body mass index (BMI) across the rest of the BMI spectrum relate to CVD risk factors and whether adult BMI affects these associations. Our aim was to examine associations between childhood BMI trajectories and adult CVD risk factors. METHODS: We included 2466 individuals with childhood weights and heights (ages 6-14) from the Copenhagen School Health Records Register and adult CVD risk factors (ages

20-81) from the Copenhagen City Heart Study. Associations between childhood BMI trajectories identified by latent class modelling and CVD risk factors were examined using generalized linear regression analyses with and without adjustment for adult BMI. Normal-weight and overweight were defined by growth references from the Centers for Disease Control and Prevention. RESULTS: We identified four childhood trajectories within the normal-weight spectrum and one trajectory of overweight. Compared to the trajectory with the lowest BMI level, several higher BMI trajectories were associated with worse circumference, HDL and glucose homeostasis in adulthood. The highest trajectory was additionally associated with higher total cholesterol and triglycerides. When adjusting for adult BMI, the higher BMI trajectories had lower waist circumference, blood pressure and triglycerides. CONCLUSIONS: Trajectories of BMI within the normal-weight range and in the overweight range are associated with a worse CVD risk profile than in the lowest BMI trajectory, and these associations are modifiable by growth after childhood.

[6] *Harada-Shiba M, Ali S, Gipe DA et al.* **A randomized study investigating the safety, tolerability, and pharmacokinetics of evinacumab, an ANGPTL3 inhibitor, in healthy Japanese and Caucasian subjects**. Atherosclerosis 2020; 314:33-40.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33130482
ABSTRACT
BACKGROUND AND AIMS: Evinacumab, an angiopoietin-like protein 3 monoclonal antibody, reduced low-density lipoprotein cholesterol (LDL-C) significantly in a Phase 2 study of patients with homozygous familial hypercholesterolemia. In this double-blind, placebo-controlled Phase 1 study, we compared safety, tolerability, pharmacokinetics, and pharmacodynamics of evinacumab between healthy Japanese and Caucasian adults. METHODS: Subjects with LDL-C ≥2.6 and <4.1 mmol/L were enrolled to one of four dose cohorts: evinacumab subcutaneous (SC) 300 mg single dose, SC 300 mg once weekly for eight doses, intravenous (IV) 5 mg/kg, or IV 15 mg/kg once every 4 weeks for two doses. Each cohort comprised 24 subjects (12 Japanese; 12 Caucasian), randomized (3:1) to receive evinacumab or placebo within each ethnic group with a 24-week follow-up. RESULTS: The safety profile of evinacumab (IV and SC) in both ethnicities was comparable with placebo, with no serious or severe treatment-emergent adverse events. Pharmacokinetic profiles were comparable between Japanese and Caucasian subjects across IV and SC groups. Mean calculated LDL-C decreased from baseline with both IV doses, beginning on day 3 up to week 8. Triglyceride changes observed with evinacumab IV were rapid (seen by day 2) and sustained up to week 8. Evinacumab SC doses also reduced LDL-C and triglyceride levels, although lower doses induced smaller changes. Evinacumab (IV and SC) reduced other lipids, including apolipoprotein B, versus placebo. CONCLUSIONS: In both ethnicities, evinacumab (IV and SC) was generally well tolerated, exhibiting comparable pharmacokinetic profiles. Dose-related reductions in LDL-C and triglycerides were observed with evinacumab in both ethnic groups.

[7] *Pan L, Liao YH, Mo MQ et al.* **CMIP SNPs and their haplotypes are associated with dyslipidaemia and clinicopathologic features of IgA nephropathy**. Bioscience reports 2020; 40.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33112407
ABSTRACT

The relationship between serum lipid profiles and related clinicopathologic features of IgA nephropathy (IgAN) and c-Maf-inducing protein (CMIP) gene polymorphisms is unclear. The present study was designed to examine the effect of CMIP single-nucleotide polymorphisms (SNPs) on dyslipidaemia and clinicopathologic features of IgAN. Clinical and pathological data from patients with IgAN diagnosed at the First Affiliated Hospital of Guangxi Medical University were collected. DNA was extracted from blood samples. CMIP rs2925979 and CMIP rs16955379 genotypes were determined by PCR and direct sequencing. Among 543 patients, 281 had dyslipidaemia (51.7%). Compared with the non-dyslipidaemia group, the dyslipidaemia group exhibited higher blood pressure, blood urea nitrogen, uric acid, and body mass index; higher prevalence of oedema, haematuria, tubular atrophy, and interstitial fibrosis; and lower albumin and estimated glomerular filtration rate. In the dyslipidaemia group, the frequency of C allele carriers was higher than that of non-C allele carriers for rs16955379. Multivariate linear regression analysis showed that total cholesterol, low-density lipoprotein and high-density lipoprotein were associated with rs16955379C allele carriers. Apolipoprotein B was associated with A allele carriers of rs2925979. Linkage disequilibrium was observed between rs16955379 and rs2925979, and rs2925979G-rs16955379T was the most common haplotype. The frequencies of the four CMIP SNP haplotypes differed between dyslipidaemia and non-dyslipidaemia groups in IgAN ($P<0.05$, for all above). Dyslipidaemia is a common complication in IgAN patients, and those with dyslipidaemia present poor clinicopathologic features. CMIP SNPs and their haplotypes are closely correlated with the occurrence of dyslipidaemia and clinicopathologic damage in IgAN patients.

[8] *Bolek T, Samoš M, Stančiaková L et al.* **The impact of atorvastatin on dabigatran plasma levels in patients with atrial fibrillation**. Blood coagulation & fibrinolysis : an international journal in haemostasis and thrombosis 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33122496
ABSTRACT

[9] *Wagner N, Wagner KD*. **The Role of PPARs in Disease**. Cells 2020; 9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33126411
ABSTRACT
Peroxisome proliferator-activated receptors (PPARs) are nuclear receptors that function as ligand-activated transcription factors. They exist in three isoforms: PPARα, PPARβ/δ, and PPARγ. For all PPARs, lipids are endogenous ligands, linking them directly to metabolism. PPARs form heterodimers with retinoic X receptors, and upon ligand binding, they modulate the gene expression of downstream target genes, depending on the presence of co-repressors or co-activators. This results in a complex, cell type-specific regulation of proliferation, differentiation, and cell survival. PPARs are linked to metabolic disorders and are interesting pharmaceutical targets. PPARα and PPARγ agonists are already in clinical use for the treatment of hyperlipidemia and type 2 diabetes, respectively. More recently, PPARβ/δ activation came into focus as an interesting novel approach for the treatment of metabolic syndrome and associated cardiovascular diseases; however, this has been limited due to the highly controversial function of PPARβ/δ in cancer. This Special Issue of Cells brings together the most recent advances in understanding the various aspects of the action of PPARs, and it provides new insights into our understanding of PPARs, implying also the latest therapeutic perspectives for the utility of PPAR modulation in different disease settings.

[10] *Marston NA, Ruff CT, Sabatine MS*. **Response by Marston et al to Letter Regarding Article, "The Effect of PCSK9 (Proprotein Convertase Subtilisin/Kexin Type 9) Inhibition on the Risk of Venous Thromboembolism"**. Circulation 2020; 142:e264.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33104403
ABSTRACT

[11] *Qi Z, Sun A, Ge J*. **Letter by Qi et al Regarding Article, "The Effect of PCSK9 (Proprotein Convertase Subtilisin/Kexin Type 9) Inhibition on the Risk of Venous Thromboembolism"**. Circulation 2020; 142:e262-e263.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33104398
ABSTRACT

[12] *Zhao Z, Yang Y, Wang J et al.* **Combined treatment with valsartan and fluvastatin to delay disease progression in nonpermanent atrial fibrillation with hypertension: A clinical trial**. Clinical cardiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33103770
ABSTRACT
BACKGROUND: Atrial fibrillation (AF) is a complex cardiac arrhythmia in clinical practice with increasing incidence. However, the effects of statins on patients with AF are not quite clear. HYPOTHESIS: To investigate the protective effect of calcium channel blocker (CCB) and valsartan combined fluvastatin on hypertension (HTN) patients with nonpermanent AF. METHODS: In three and a half years, 189 cases of patients diagnosed as HTN combining nonpermanent AF by eight medical centers, were recruited and randomly assigned to four groups with varied treatments: CCB group; CCB + statin group; valsartan group; and valsartan + statin group. The four groups were followed up for 24 months. The 7-day Holter ultrasound echocardiography (UCG) and biochemical indexes were completed at preset time nodes respectively. RESULTS: After 24 months of follow-up, 178 patients completed the study. Compared with CCB group, the blood lipid level, inflammatory index, ultrasonic index and electrocardiographic measurement results of CCB + statin group, valsartan group and valsartan + statin group were improved in different degrees and had statistical significance ($P < .05$ or $P < .01$). Furthermore, the improvement trend of CCB + statin group and valsartan + statin group was more obvious. CONCLUSIONS: The results indicated that valsartan can reduce AF load and recurrence rate, and delay the progression of nonpermanent AF to permanent AF in multiple ways, and the effect of combination of valsartan and fluvastatin is more significant. These results provide a new direction for the integrated upstream control strategy of AF.

[13] *Fernandez-Prado R, Perez-Gomez MV, Ortiz A*. **Pelacarsen for lowering lipoprotein(a): implications for patients with chronic kidney disease**. Clinical kidney journal 2020; 13:753-757.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33123354
ABSTRACT
Chronic kidney disease (CKD) patients are at an increased risk of cardiovascular disease (CVD) and statins may not be protective in advanced CKD. The reasons for the limited efficacy of statins in advanced CKD are unclear, but statins may increase plasma levels of the highly

atherogenic molecule lipoprotein(a), also termed Lp(a), as well as PCSK9 (protein convertase subtilisin/kexin type 9) levels. Lp(a) has also been linked to calcific aortic stenosis, which is common in CKD. Moreover, circulating Lp(a) levels increase in nephrotic syndrome with declining renal function and are highest in patients on peritoneal dialysis. Thus, the recent publication of the Phase 2 randomized controlled trial of pelacarsen [also termed AKCEA-APO(a)-LRx and TQJ230], a hepatocyte-directed antisense oligonucleotide targeting the LPA gene messenger RNA, in persons with CVD should be good news for nephrologists. Pelacarsen safely and dose-dependently decreased Lp(a) levels by 35-80% and a Phase 3 trial [Lp(a)HORIZON, NCT04023552] is planned to run from 2020 to 2024. Unfortunately, patients with estimated glomerular filtration rate <60 mL/min or urinary albumin:creatinine ratio >100 mg/g were excluded from Phase 2 trials and those with 'significant kidney disease' will be excluded from the Phase 3 trial. Optimized exclusion criteria for Lp(a)HORIZON would provide insights into the role of Lp(a) in CVD in CKD patients.

[14] *Courlet P, Guidi M, Alves Saldanha S et al.* **Pharmacokinetic/Pharmacodynamic Modelling to Describe the Cholesterol Lowering Effect of Rosuvastatin in People Living with HIV**. Clinical pharmacokinetics 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33124006

ABSTRACT

BACKGROUND: Rosuvastatin is a lipid-lowering agent widely prescribed in people living with HIV, which is actively transported into the liver, making it a potential victim of drug-drug interactions with antiretroviral agents. OBJECTIVES: The aims of this study were to characterise the pharmacokinetic profile of rosuvastatin and to describe the relationship between rosuvastatin concentrations and non-high-density lipoprotein (HDL)-cholesterol levels in people living with HIV. METHODS: A population pharmacokinetic model (NONMEM) was developed to quantify the influence of demographics, clinical characteristics and comedications on rosuvastatin pharmacokinetics. This model was combined with an indirect effect model to describe non-HDL-cholesterol measurements. RESULTS: A two-compartment model with sequential zero- and first-order absorption best fitted the 154 rosuvastatin concentrations provided by 65 people living with HIV. None of the tested covariates significantly influenced rosuvastatin pharmacokinetics. A total of 403 non-HDL cholesterol values were available for pharmacokinetic-pharmacodynamic modelling. Baseline non-HDL cholesterol decreased by 14% and increased by 12% with etravirine and antiretroviral drugs with a known impact on the lipid profile (i.e. protease inhibitors, efavirenz, cobicistat), respectively. The baseline value was surprisingly 43% lower in people living with HIV aged 80 years compared with those aged 40 years. Simulations based on the covariate-free model predicted that, under standard rosuvastatin dosages of 5 mg and 20 mg once daily, 31% and 64% of people living with HIV would achieve non-HDL-cholesterol targets, respectively. CONCLUSIONS: The high between-subject variability that characterises both rosuvastatin pharmacokinetic and pharmacodynamic profiles remained unexplained after the inclusion of usual covariates. Considering its limited potential for drug-drug interactions with antiretroviral agents and its potent lipid-lowering effect, rosuvastatin prescription appears safe and effective in people living with HIV with hypercholesterolaemia. CLINICAL TRIAL REGISTRATION NO: NCT03515772.

[15] *Fisher R, Vandehei A, Haller C et al.* **Reporting the Presence of Coronary Artery Calcium in the Final Impression of Non-gated CT Chest Scans Increases the Appropriate Utilization of Statins**. Cureus 2020; 12:e10579.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33110715

ABSTRACT

Background Coronary artery calcium (CAC) scoring based on gated non-contrast cardiac computed tomography (CT) is a validated risk marker of major adverse cardiovascular events (MACE). Reporting of CAC on non-gated CT chest (NGCT) scans and the impact on medical therapy is not well studied. Methods A retrospective cohort of 5,043 NGCT scans was reviewed for the presence of CAC. The radiology report was reviewed to determine whether CAC was mentioned in either the body of the report or the final impression. Electronic medical records (EMR) were abstracted for baseline demographics, cardiovascular (CV) risk factors, lipid-lowering agents, and aspirin (ASA) prior to and after NGCT. Results CAC was present in 63.0% of NGCT scans. Of these scans, CAC was mentioned in the body of the report in 81.6% of studies. Conversely, CAC was mentioned in the final impressions in only 15.1% of these scans. Amongst patients with CAC, initiation of a statin in treatment-naive patients was more common when CAC was mentioned in the final impression versus the body only (12.3% vs. 4.9%, p=0.001) despite the fact that baseline utilization of statins in this cohort was higher (71.1% vs. 64.1%, p=0.005). Initiation of a statin in treatment-naive patients had a trend towards significance when CAC was mentioned in the body of the report versus not reported (4.9% vs. 2.62%, p=0.142). Reporting of CAC in the final impression significantly increased the initiation of ASA in treatment-naive patients (9.52% vs. 4.33%, p=0.033). Reporting of CAC in either the final impression or the body of the report did not affect the initiation of non-statin lipid-lowering therapies in patients with CAC. Conclusion The inclusion of CAC in the final impression of NGCT radiology reports positively impacts the appropriate initiation of statin and aspirin therapy in treatment-naive patients. Universal adherence to a standardized reporting system for the presence of CAC on NGCT should be considered to improve the initiation of guideline-directed medical therapy.

[16] *Xu RX, Zhang Y, Zhang Y et al.* **Effects of Pitavastatin on Lipoprotein Subfractions and Oxidized Low-density Lipoprotein in Patients with Atherosclerosis**. Current medical science 2020; 40:879-884.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33123903

ABSTRACT

It has been demonstrated that pitavastatin can significantly reduce low-density lipoprotein (LDL) cholesterol (LDL-C), but its impact on lipoprotein subfractions and oxidized low-density lipoprotein (oxLDL) has not been determined. The aim of the present study was to investigate the potential effects of pitavastatin on subfractions of LDL and high-density lipoprotein (HDL) as well as oxLDL in untreated patients with coronary atherosclerosis (AS). Thirty-six subjects were enrolled in this study. Of them, 18 patients with AS were administered pitavastatin 2 mg/day for 8 weeks and 18 healthy subjects without therapy served as controls. The plasma lipid profile, lipoprotein subfractions and circulating oxLDL were determined at baseline and 8 weeks respectively. The results showed that pitavastatin treatment indeed not only decreased LDL-C, total cholesterol (TC), triglycerides (TG) and apolipoprotein B (ApoB) levels, and increased HDL cholesterol (HDL-C), but also reduced the cholesterol concentration of all of the LDL subfractions and the percentage of intermediate and small LDL subfractions. Meanwhile,

pitavastatin could decrease plasma oxLDL levels. Furthermore, a more close correlation was found between oxLDL and LDL-C as well as LDL subfractions after pitavastatin treatment. We concluded that a moderate dose of pitavastatin therapy not only decreases LDL-C and oxLDL concentrations but also improves LDL subfractions in patients with AS.

[17] *Tham YK, Jayawardana KS, Alshehry ZH et al.* **Novel Lipid Species for Detecting and Predicting Atrial Fibrillation in Patients with Type 2 Diabetes**. Diabetes 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33115826
ABSTRACT
The incidence of atrial fibrillation (AF) is higher in patients with diabetes. The goal of this study was to assess if the addition of plasma lipids to traditional risk factors could improve the ability to detect and predict future AF in patients with type 2 diabetes. Logistic regression models were used to identify lipids associated with AF/future AF from plasma lipids (n=316) measured from participants from the ADVANCE trial (n=3,772). To gain mechanistic insight, follow-up lipid analysis was undertaken in a mouse model which has an insulin-resistant heart and is susceptible to AF. Sphingolipids, cholesteryl esters and phospholipids were associated with AF prevalence, whereas two G(M3) ganglioside species were associated with future AF. For AF detection and prediction, addition of 6 and 3 lipids, respectively, to a base model (12 conventional risk factors) increased the C-statistics (detection:0.661 to 0.725; prediction:0.674 to 0.715), and categorical net reclassification indices. GM3(d18:1/24:1) was lower in patients who developed AF, improved the C-statistic for the prediction of future AF, and was lower in the plasma of the mouse model susceptible to AF. This study demonstrates that plasma lipids have the potential to improve both the detection and prediction of AF in patients with diabetes.

[18] *Hong T, Su Q, Li X et al.* **Glucose-lowering pharmacotherapies in Chinese adults with type 2 diabetes and cardiovascular disease or chronic kidney disease. An expert consensus reported by the Chinese Diabetes Society and the Chinese Society of Endocrinology**. Diabetes/metabolism research and reviews 2020:e3416.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33120435
ABSTRACT
Patients with type 2 diabetes mellitus (T2DM) are at risk of developing atherosclerotic cardiovascular disease (ASCVD) and chronic kidney disease (CKD), which are important causes of disabling and death in patients with T2DM. For the prevention and management of ASCVD or CKD, cardiovascular risk factors should be systematically evaluated, and ASCVD and CKD should be screened in patients with T2DM. In this consensus, we recommended that metformin should be used as the first-line therapy for patients with T2DM and ASCVD or very high cardiovascular risk, heart failure (HF) or CKD, and should be retained in the treatment regimen unless contraindicated or not tolerated. In patients with T2DM and established ASCVD or very high cardiovascular risk, addition of a glucagon-like peptide 1 receptor agonist (GLP-1RA) or sodium-glucose cotransporter type 2 (SGLT2) inhibitor with proven cardiovascular benefits should be considered independent of individualised glycated haemoglobin (HbA(1C)) targets. In patients with T2DM and HF, an SGLT2 inhibitor should be preferably added regardless of HbA(1C) levels. In patients with T2DM and CKD, SGLT2 inhibitors should be preferred for the combination therapy independent of individualised HbA(1C) targets, and GLP-1RAs with proven renal benefits would be alternative if SGLT2 inhibitors are contraindicated. Moreover, the prevention of hypoglycaemia and management of

multiple risk factors by comprehensive regimen, including lifestyle intervention, antihypertensive therapies, lipid-lowering treatment and antiplatelet therapies, should be kept in mind in treating patients with T2DM and ASCVD, HF or CKD.

[19] *Le TD, Nguyen NPT, Nguyen ST et al.* **The Association Between Femoral Artery Intima-Media Thickness and Serum Glucagon-Like Peptide-1 Levels Among Newly Diagnosed Patients with Type 2 Diabetes Mellitus**. Diabetes, metabolic syndrome and obesity : targets and therapy 2020; 13:3561-3570.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33116707
ABSTRACT
INTRODUCTION: Endothelium dysfunction and decrease of incretin effects occur early in type 2 diabetes mellitus and these changes contribute to diabetic cardiovascular complications such as atherosclerosis, thick intima-media, coronary, and peripheral arterial diseases. In patients with diabetes, the femoral artery is a site of a high incidence of injury in peripheral vascular diseases, and atherosclerotic changes may appear earlier in the femoral artery compared to the carotid artery. This study was conducted to determine the prevalence of increased femoral artery intima-media thickness (IMT) and atherosclerotic plaque and their correlation with serum glucagon-like peptide-1 (GLP-1) levels in newly-diagnosed patients with type 2 diabetes mellitus. MATERIALS AND METHODS: A cross-sectional study was conducted on 332 patients with nT2D in the National Endocrinology Hospital, Vietnam from January 2015 to May 2018. IMT was measured by Doppler ultrasound and GLP-1 by enzyme-linked immunosorbent assay (ELISA). All data were analyzed with SPSS version 26 for Windows (SPSS Inc, Chicago, IL). RESULTS: Prevalence of thick femoral artery IMT and atherosclerotic plaque was 38.2 and 22.3%, respectively. There was a relationship between IMT and age, waist to hip ratio (WHR), systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting GLP-1, high sensitive CRP (hsCRP) and 24-hour microalbuminuria secretion (24-h MAUS). The fasting serum GLP-1 (fGLP-1) levels were reduced significantly in patients with thickness and atherosclerosis femoral artery ($p = 0.001$). After adjusting with other related factors, namely, DBP and estimated glomerular filtration rate (eGFR), whilst hsCRP and 24-h MAUS showed a significantly positive correlation to IMT (Standardized B and p of 0.242, 0.004 and 0.178, 0.043, respectively), fGLP-1 showed a significantly negative correlation to IMT (Standardized B = -0.288, $p = 0.001$). CONCLUSION: Among n2TD, the percentage for femoral artery thick IMT and atherosclerosis was 38.2% and 22.3% respectively, and serum GLP-1 was negatively correlated with thick IMT and atherosclerosis.

[20] *Yuan T, Liu S, Dong Y et al.* **Effects of dapagliflozin on serum and urinary uric acid levels in patients with type 2 diabetes: a prospective pilot trial**. Diabetology & metabolic syndrome 2020; 12:92.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33117454
ABSTRACT
BACKGROUND: We aimed to evaluate the effects of short-term therapy with dapagliflozin on serum uric acid (SUA) and urinary uric acid (UUA) levels in patients with type 2 diabetes. METHODS: In this prospective pilot trial, 8 patients with type 2 diabetes mellitus were assigned to the treatment group with dapagliflozin 10 mg once daily for one week, and 7 subjects with normal glucose tolerance were recruited into the control group. Data of anthropometric measurements, SUA, 24-h UUA, fractional excretion of UA (FEUA), serum lipid

parameters and 3-h oral glucose tolerance test (OGTT) were collected in both treatment and control groups; all examinations were repeated after treatment. The area under the curve of glucose (AUC(Glu)) was calculated to reflect the general glucose levels, while insulin resistance and islet β-cell function were reflected by indexes calculated according to the data obtained from the OGTT. RESULTS: The weight and serum lipid parameters showed no differences before and after treatment with dapagliflozin for one week. We found SUA levels decreased from 347.75 ± 7.75 μmol/L before treatment to 273.25 ± 43.18 μmol/L after treatment, with a statistically significant difference (P = 0.001) and was accompanied by a significant increase in FEUA from 0.009 to 0.029 (P = 0.035); there was a linear correlation between SUA and FEUA levels. Glucose control, insulin sensitivity and islet β-cell function were improved to a certain extent. We also found a positive correlation between the decrease in glucose levels and the improvement in islet β-cell function. CONCLUSIONS: The SUA-lowering effect of dapagliflozin could be driven by increasing UA excretion within one week of treatment, and a certain degree of improvement in glucose levels and islet β-cell function were observed.Trial registration ClinicalTrials.gov identifier, NCT04014192. Registered 12 July 2019, https://www.clinicaltrials.gov/ct2/show/NCT04014192:term=NCT04014192&draw=2&rank=1. Yes.

[21] *Kaur H, Singh J, Kashyap JR et al.* **Relationship Between Statin-associated Muscle Symptoms, Serum Vitamin D and Low-density Lipoprotein Cholesterol - A Cross-sectional Study**. European endocrinology 2020; 16:137-142.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33117445

ABSTRACT

INTRODUCTION: Statin-associated muscle symptoms (SAMS) can lead to medication non-adherence among statin users. There is a complex relationship between SAMS, vitamin D and low-density lipoprotein cholesterol (LDL-C). The objective of this study was to evaluate the relationship between vitamin D, LDL-C and occurrence of SAMS. METHODS: This was a cross-sectional study in patients using statins. Thorough patient histories were taken, a clinical examination was conducted and SAMS were recorded. Levels of vitamin D, creatine phosphokinase (CPK) and LDL-C were measured. These parameters were compared amongst statin users with SAMS and those without SAMS. Levels of vitamin D and LDL-C were converted into percentiles and their relationship with SAMS was evaluated in terms of odds ratio. Receiver operating characteristics (ROC) were drawn, taking vitamin D and LDL-C as predictors of SAMS. RESULTS: A total of 121 statin users were enrolled in this study. Thirty-eight patients (31.4%) presented with SAMS. Significantly lower levels of serum vitamin D were observed amongst statin users with SAMS compared with those without SAMS (19.8 ± 9.67 ng/mL versus 25.0 ± 14.6 ng/mL; 95% confidence interval -10.4 to -0.07; p=0.04). With vitamin D levels less than or equal to 5th, 10th and 25th percentile, the chances of occurrence of SAMS were significantly higher, but not at the 50th percentile (corresponding vitamin D level of 20.21 ng/mL). LDL-C did not show any conclusive relationship with SAMS. ROC curves showed a significant discrimination for vitamin D levels, but not for LDL-C. CONCLUSION: Statin users with low levels of vitamin D are at increased risk of developing SAMS. However, LDL-C status of statin users failed to predict any meaningful association with SAMS. Given the small sample size of this study, these results should be regarded as preliminary.

[22] *Zambon A, Mello ESA, Farnier M*. **The burden of cholesterol accumulation through the lifespan: why pharmacological intervention should start earlier to go further?** European heart journal. Cardiovascular pharmacotherapy 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33119073
ABSTRACT
Among the cardiovascular risk factors, cholesterol-rich atherogenic lipoproteins play a central role in the pathogenesis of atherosclerosis. In middle-aged adults, the size of the total atherosclerotic plaque burden is influenced by both the concentration of circulating atherogenic lipoproteins and by the total duration of exposure to these lipoproteins. This review describes the evidence supporting a causal link between life-long elevations in atherogenic lipoproteins and future risk of atherosclerosis; evidence strengthened by recent epidemiological, genetic and clinical data. By consequence, adolescence and early adulthood are a crucial time for determining later cardiovascular disease risk. Arguments showing that early optimal lipid control leads to improved outcomes will be presented, and suggestions put forward for how those most at risk should be identified and managed.

[23] *Leclercq T, Falcon-Eicher S, Farnier M et al.* **A case report of an acute coronary syndrome in a 10-year-old boy with homozygous familial hypercholesterolaemia**. European heart journal. Case reports 2020; 4:1-5.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33123673
ABSTRACT
BACKGROUND: Familial hypercholesterolaemia is a well-known disorder, but clinical diagnoses tend to be delayed. Acute coronary syndrome may occur in childhood. CASE SUMMARY: Our patient, a young boy with homozygous familial hypercholesterolaemia, complained of persistent chest pain at rest and suffered a non-ST-elevation myocardial infarction (NSTEMI). The diagnosis of NSTEMI was made on the basis of his clinical features, dynamic electrocardiogram changes, troponin elevation, and cardiac computed tomography findings. The patient was managed surgically by intrathoracic artery (ITA) bypass graft. During post-operative follow-up, the young patient suffered from angina pectoris from unexpected and exceptional atheroma stenosis on the ITA. DISCUSSION: Familial hypercholesterolaemia needs to be identified quickly in young patients and lipid lowering therapies should be started without delay.

[24] *Paz-Graniel I, Babio N, Becerra-Tomás N et al.* **Association between coffee consumption and total dietary caffeine intake with cognitive functioning: cross-sectional assessment in an elderly Mediterranean population**. European journal of nutrition 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33125576
ABSTRACT
PURPOSE: Coffee is rich in compounds such as polyphenols, caffeine, diterpenes, melanoidins and trigonelline, which can stimulate brain activity. Therefore, the possible association of coffee consumption with cognition is of considerable research interest. In this paper, we assess the association of coffee consumption and total dietary caffeine intake with the risk of poor cognitive functioning in a population of elderly overweight/obese adults with metabolic syndrome (MetS). METHODS: PREDIMED-plus study participants who completed the Mini-Mental State Examination test (MMSE) (n = 6427; mean age = 65 ± 5 years) or a

battery of neuropsychological tests were included in this cross-sectional analysis. Coffee consumption and total dietary caffeine intake were assessed at baseline using a food frequency questionnaire. Logistic regression models were fitted to evaluate the association between total, caffeinated and decaffeinated coffee consumption or total dietary caffeine intake and cognitive impairment. RESULTS: Total coffee consumers and caffeinated coffee consumers had better cognitive functioning than non-consumers when measured by the MMSE and after adjusting for potential confounders (OR 0.63; 95% CI 0.44-0.90 and OR 0.56; 95% CI 0.38-0.83, respectively). Results were similar when cognitive performance was measured using the Clock Drawing Test (CDT) and Trail Making Test B (TMT-B). These associations were not observed for decaffeinated coffee consumption. Participants in the highest tertile of total dietary caffeine intake had lower odds of poor cognitive functioning than those in the reference tertile when screened by the MMSE (OR 0.64; 95% CI 0.47-0.87) or other neurophysiological tests evaluating a variety of cognitive domains (i.e., CDT and TMT-A). CONCLUSIONS: Coffee consumption and total dietary caffeine intake were associated with better cognitive functioning as measured by various neuropsychological tests in a Mediterranean cohort of elderly individuals with MetS. TRIAL REGISTRATION: ISRCTN89898870. Registration date: July 24, 2014.

[25] *Zhang Q, Dong J, Yu Z*. **Pleiotropic use of Statins as non-lipid-lowering drugs**. International journal of biological sciences 2020; 16:2704-2711.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33110390
ABSTRACT
Statins, known as HMG-CoA reductase (HMGCR) inhibitors, have primarily been utilized for metabolic and angiographic medical applications because of their cholesterol-lowering effects. Similar to other drugs, statins may also induce a series of potential side effects. Statins inhibit the HMGCR (rate-limiting enzyme) activity in early stages of mevalonate pathway and then indirectly affect a number of intermediate products, including non-sterol isoprenoids (coenzyme Q10, dolichol etc.), which can result in impaired functions of body organs. Recently, scores of studies have uncovered additional functional mechanisms of statins in other diseases, such as diabetes mellitus, nervous system diseases, coronary heart disease, inflammation and cancers. This review aims to summarize the positive and adverse mechanisms of statin therapy. Statin care should be taken in the treatment of many diseases including cancers. Since the underlying mechanisms are not fully elucidated, future studies should spend more time and efforts on basic research to explore the mechanisms of statins.

[26] *Lei YF, Lin HC, Lin HL et al.* **Association Between Use of Antihyperlipidemic Agents and Chronic Obstructive Pulmonary Disease in Patients with Hyperlipidemia: A Population-Based Retrospective Cohort Study**. International journal of chronic obstructive pulmonary disease 2020; 15:2573-2581.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33116474
ABSTRACT
OBJECTIVE: The effect of statins and fibrates on the risk of chronic obstructive pulmonary disease (COPD) remains unclear. The aim of this study was to investigate the effects of statins and fibrates on the risk of COPD in patients with hyperlipidemia. PATIENTS AND METHODS: This study involved a retrospective cohort with a follow-up period of 6 years. We identified patients who were diagnosed as having hyperlipidemia between 2000 and 2016 from Taiwan's

National Health Insurance Research Database. A Cox proportional hazard model was used to estimate the risk of COPD among different groups. The dose-related effects of statins and fibrates on the risk of COPD were evaluated according to the defined daily dose (DDD). RESULTS: Patients with hyperlipidemia not using statins and fibrates (group II) had a significantly higher risk of COPD compared with their comparison group, with an adjusted hazard ratio (HR) of 1.091 [95% confidence interval (CI): 1.034-1.152, $p < 0.01$]. Dose-dependent reduction in the risk of COPD was observed in patients with hyperlipidemia using statins or fibrates compared with patients not using them. Moreover, with an increase in cumulative exposure, a reduced risk of COPD was observed in patients using more than 361 DDDs, with an adjusted HR of 0.474 (95% CI: 0.401-0.559, $p < 0.001$). Patients on fibrate monotherapy using more than 541 DDDs were observed to have an adjusted HR of 0.454 (95% CI: 0.226-0.910, $p < 0.05$) and those on statin monotherapy with over 361 DDDs were noted to have an adjusted HR of 0.583 (95% CI: 0.459-0.740, $p < 0.001$). CONCLUSION: This study demonstrated that an increase in the cumulative exposure of statins and fibrates significantly reduced the risk of COPD in patients with hyperlipidemia, and the risk reduction appeared to be significantly dose dependent.

[27] *Blasetti A, Franchini S, Castorani V et al.* **Skipping Breakfast Is Associated with an Atherogenic Lipid Profile in Overweight and Obese Prepubertal Children**. Int J Endocrinol 2020; 2020:1849274.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33101407
ABSTRACT
BACKGROUND: Skipping breakfast has been associated with a higher risk of obesity and cardiovascular (CV) risk factors. However, it is not known if skipping breakfast is also correlated with CV risk factors independently from obesity. The mechanisms explaining the role of skipping breakfast on promoting fat accumulation as well as CV risk are not known. Hormones, in particular, insulin-like growth factor-1 (IGF-1), may potentially play a role in the metabolic profile of breakfast skippers. AIM: This cross-sectional study aims to test, in a sample of overweight/obese children, the hypotheses that skipping breakfast is associated with a worse metabolic profile and that IGF-1 levels are associated with this unfavorable metabolic profile. METHODS AND RESULTS: We enrolled 112 overweight/obese prepubertal children (3-12 years). Anthropometric characteristics (height SDS, weight SDS, and body mass index (BMI) z-score) were measured. Blood samples were collected to evaluate glucose and lipid metabolisms and hormone profile (growth hormone (GH), IGF-1, insulin, and cortisol). The triglycerides/high-density lipoprotein (HDL) cholesterol ratio was calculated as a predictor of cardiovascular risk. Children were divided into two groups according to breakfast habits: consumers (≥5 weekly; N = 76) and skippers (≤4 weekly; N = 36). Glycaemia, total and low-density lipoprotein (LDL) cholesterol, triglycerides ($p < 0.05$), and triglycerides/HDL cholesterol ratio ($p < 0.001$) were higher, while HDL cholesterol was lower ($p < 0.01$) in skippers as compared to consumers. IGF-1 concentrations were inversely correlated with LDL cholesterol ($r = -0.279$, $p=0.013$) and directly correlated with HDL cholesterol ($r = 0.226$, $p=0.047$). IGF-1 correlated positively with HDL cholesterol ($r = 0.266$, $p=0.045$) in consumers and correlated negatively with LDL cholesterol ($r = -0.442$, $p=0.024$) in skippers. Breakfast consumption among prepubertal overweight/obese children showed a better lipid profile in comparison with those who skipped breakfast [OR: 0.165 (95% CI: 0.053-0.518), $p=0.001$]; these latter odds of the increased triglycerides/HDL cholesterol ratio was 6.1-fold higher. CONCLUSIONS:

Breakfast skippers show a worse lipid profile when compared to breakfast consumers. IGF-1 might play a role as an independent modulator of lipid metabolism.

[28] *Cianflone E, Cappetta D, Mancuso T et al.* **Statins Stimulate New Myocyte Formation After Myocardial Infarction by Activating Growth and Differentiation of the Endogenous Cardiac Stem Cells**. International journal of molecular sciences 2020; 21.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33114544

ABSTRACT

The 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins) exert pleiotropic effects on cardiac cell biology which are not yet fully understood. Here we tested whether statin treatment affects resident endogenous cardiac stem/progenitor cell (CSC) activation in vitro and in vivo after myocardial infarction (MI). Statins (Rosuvastatin, Simvastatin and Pravastatin) significantly increased CSC expansion in vitro as measured by both BrdU incorporation and cell growth curve. Additionally, statins increased CSC clonal expansion and cardiosphere formation. The effects of statins on CSC growth and differentiation depended on Akt phosphorylation. Twenty-eight days after myocardial infarction by permanent coronary ligation in rats, the number of endogenous CSCs in the infarct border zone was significantly increased by Rosuvastatin-treatment as compared to untreated controls. Additionally, commitment of the activated CSCs into the myogenic lineage (c-kit(pos)/Gata4(pos) CSCs) was increased by Rosuvastatin administration. Accordingly, Rosuvastatin fostered new cardiomyocyte formation after MI. Finally, Rosuvastatin treatment reversed the cardiomyogenic defects of CSCs in c-kit haploinsufficient mice, increasing new cardiomyocyte formation by endogenous CSCs in these mice after myocardial infarction. In summary, statins, by sustaining Akt activation, foster CSC growth and differentiation in vitro and in vivo. The activation and differentiation of the endogenous CSC pool and consequent new myocyte formation by statins improve myocardial remodeling after coronary occlusion in rodents. Similar effects might contribute to the beneficial effects of statins on human cardiovascular diseases.

[29] *Nakamura M, Yamamoto Y, Imaoka W et al.* **Relationships between Smoking Status, Cardiovascular Risk Factors, and Lipoproteins in a Large Japanese Population**. Journal of atherosclerosis and thrombosis 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33116031

ABSTRACT

AIMS: Smoking is a major risk factor for cardiovascular disease (CVD), a leading cause of death and disability. Other CVD risk factors include age, gender, hypertension, diabetes, increased low-density lipoprotein cholesterol (LDL-C) and decreased high-density lipoprotein cholesterol (HDL-C). Our goal was to assess relationships between smoking status and CVD risk factors, with a focus on direct LDL-C, HDL-C, triglycerides (TG) and small dense LDL-C (sdLDL-C). METHODS: A total of 34,497 Japanese men and women, mean age 51 years, had their CVD risk factors including fasting serum total cholesterol, TG, HDL-C, sdLDL-C, and direct LDL-C assessed. One-way ANOVA and multiple linear regression analyses were carried to assess the interrelationships of these parameters with smoking. RESULTS: In both men and women, current smokers had significantly ($p < 0.001$) higher median TG (+19.6%, +16.9%) and sdLDL-C levels (+12.7%, +4.2%) levels, and significantly ($p < 0.001$) lower HDL-C levels (-

7.3%, -4.3%) than non-smokers. They were also significantly ($p < 0.05$) more likely to have TG values > 150 mg/dL (+56.8%, +116.3%), sdLDL-C > 40.1 mg/dL (+28.8%, +44.9%), and HDL-C < 40 mg/dL (+89.8%, +114.3%). Ex-smokers generally had lipid values that were intermediate between non-smokers and current smokers. Multivariate analysis confirmed the significance of these relationships. CONCLUSION: Our data indicate that current cigarette smoking is associated with increased TG and sdLDL-C levels, as well as decreased HDL-C levels. Furthermore, smoking effect on lipid profiles remain after cessation. These data provide further justification for smoking cessation.

[30] *Musetti B, González-Ramos H, González M et al.* **Cannabis sativa extracts protect LDL from Cu(2+)-mediated oxidation**. J Cannabis Res 2020; 2.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33123676

ABSTRACT

BACKGROUND: Multiple therapeutic properties have been attributed to Cannabis sativa. However, further research is required to unveil the medicinal potential of Cannabis and the relationship between biological activity and chemical profile. OBJECTIVES: The primary objective of this study was to characterize the chemical profile and antioxidant properties of three varieties of Cannabis sativa available in Uruguay during progressive stages of maturation. METHODS: Fresh samples of female inflorescences from three stable Cannabis sativa phenotypes, collected at different time points during the end of the flowering period were analyzed. Chemical characterization of chloroform extracts was performed by (1)H-NMR. The antioxidant properties of the cannabis sativa extracts, and pure cannabinoids, were measured in a Cu(2+)-induced LDL oxidation assay. RESULTS: The main cannabinoids in the youngest inflorescences were tetrahydrocannabinolic acid (THC-A, 242 ± 62 mg/g) and tetrahydrocannabinol (THC, 7.3 ± 6.5 mg/g). Cannabinoid levels increased more than twice in two of the mature samples. A third sample showed a lower and constant concentration of THC-A and THC (177 ± 25 and 1 ± 1, respectively). The THC-A/THC rich cannabis extracts increased the latency phase of LDL oxidation by a factor of 1.2-3.5 per µg, and slowed down the propagation phase of lipoperoxidation (IC(50) 1.7-4.6 µg/mL). Hemp, a cannabidiol (CBD, 198 mg/g) and cannabidiolic acid (CBD-A, 92 mg/g) rich variety, also prevented the formation of conjugated dienes during LDL oxidation. In fact, 1 µg of extract was able to stretch the latency phase 3.7 times and also to significantly reduce the steepness of the propagation phase (IC(50) of 8 µg/mL). Synthetic THC lengthened the duration of the lag phase by a factor of 21 per µg, while for the propagation phase showed an IC(50) ≤ 1 µg/mL. Conversely, THC-A was unable to improve any parameter. Meanwhile, the presence of 1 µg of pure CBD and CBD-A increased the initial latency phase 4.8 and 9.4 times, respectively, but did not have an effect on the propagation phase. CONCLUSION: Cannabis whole extracts acted on both phases of lipid oxidation in copper challenged LDL. Those effects were just partially related with the content of cannabinoids and partially recapitulated by isolated pure cannabinoids. Our results support the potentially beneficial effects of cannabis sativa whole extracts on the initial phase of atherosclerosis.

[31] *Brinton EA*. **Review of LDL-C Lowering with Focus on New and Emerging Agents**. The Journal of family practice 2020; 69:S69-s74.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33104111

ABSTRACT
Identify the benefits and limitations of statin therapy as a treatment option for lowering LDL-C. Intensify treatment in appropriate patients or refer for intensification. Describe the safety and efficacy of ezetimibe, bempedoic acid, PCSK9 inhibitors, LDL apheresis. Describe the safety and efficacy of medications in late-stage development or under review by the FDA for LDL-C reduction.

[32] *Johnson JT, Paul J, Cherian KE et al.* **Familial hypercholesterolemia: The skin speaks**. Journal of family medicine and primary care 2020; 9:4451-4453.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33110883
ABSTRACT
Familial hypercholesterolaemia (FH) is an autosomal dominant inherited disorder of lipoprotein metabolism caused by defects in the low-density lipoprotein receptor (LDLR) gene. It is characterized by high low-density lipoprotein (LDL) cholesterol levels, premature cardiovascular disease (CVD), and tendon xanthomas. We present the case of a 26-year-old gentleman who presented with multiple nodular eruptions over the extensor aspects of upper and lower limbs and was diagnosed as FH on the basis of positive family history, typical lipid profile abnormalities, and biopsy of the nodule consistent with tendon xanthomas. The diagnosis and management of this case is deftly feasible at the primary care level.

[33] *Yuan Y, Wu W, Sun S et al.* **PCSK9: A Potential Therapeutic Target for Sepsis**. Journal of immunology research 2020; 2020:2687692.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33123601
ABSTRACT
Sepsis is a life-threatening organ dysfunction syndrome caused by a dysregulated host response to infection. Proprotein convertase subtilisin/kexin type 9 (PCSK9) is often upregulated in the presence of sepsis and infectious diseases. In sepsis, PCSK9 degraded the low-density lipoprotein cholesterol (LDL) receptors (LDL-R) of the hepatocytes and the very low-density lipoprotein cholesterol receptors (VLDL-R) of the adipocytes, which then subsequently reduced pathogenic lipid uptake and clearance/sequestration. Moreover, it might improve cholesterol accumulation and augment toll-like receptor function in macrophages, which supported inflammatory responses. Accordingly, PCSK9 might show detrimental effects on immune host response and survival in sepsis. However, the exact roles of PCSK9 in the pathogenesis of sepsis are still not well defined. In this review, we summarized the literatures focusing on the roles of PCSK9 in sepsis. Our review provided an additional insight in the role of PCSK9 in sepsis, which might serve as a potential target for the treatment of sepsis.

[34] *Gong HY, Shi XK, Zhu HQ et al.* **Evaluation of carotid atherosclerosis and related risk factors using ultrasonic B-Flow technology in elderly patients**. J Int Med Res 2020; 48:300060520961224.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33100050
ABSTRACT
OBJECTIVE: This study was performed to identify the risk factors for carotid atherosclerotic plaque formation using B-Flow ultrasound. METHODS: In total, 120 patients who underwent bilateral carotid ultrasound examination were enrolled in this cross-sectional study. The intima-media thickness was measured, and the risk factors for carotid atheromatous plaque formation

were investigated. RESULTS: Age, sex, medical history of hypertension, coronary heart disease, and diabetes were risk factors for carotid atheromatous plaque formation. Multivariate logistic regression analysis revealed that the main risk factors for carotid atheromatous plaque formation were male sex, advanced age, a high hemoglobin concentration, a high red cell distribution width, and a high low-density lipoprotein cholesterol concentration. CONCLUSION: The risk factors for carotid atheromatous plaque formation were basically the same as those for stroke. Early ultrasound examination of the carotid artery enables the identification of risk factors associated with stroke.

[35] *Fu D, Yu JY, Connell AR et al.* **Effects of Modified Low-Density Lipoproteins and Fenofibrate on an Outer Blood-Retina Barrier Model: Implications for Diabetic Retinopathy**. Journal of ocular pharmacology and therapeutics : the official journal of the Association for Ocular Pharmacology and Therapeutics 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33107777
ABSTRACT
Purpose: There is a lack of treatment for early diabetic retinopathy (DR), including blood-retina barrier (BRB) breakdown. The robust clinical benefit of fenofibrate in DR provides an opportunity to explore disease mechanisms and therapeutic targets. We have previously found that modified lipoproteins contribute to DR and that fenofibrate protects the inner BRB. We now investigate (1) whether modified lipoproteins elicit outer BRB injury and (2) whether fenofibrate may alleviate such damage. Methods: Human retinal pigment epithelium ARPE-19 cells were cultured in semipermeable transwells to establish a monolayer barrier and then exposed to heavily oxidized, glycated low-density lipoprotein (HOG-LDL, 25-300 mg/L, up to 24 h) versus native (N)-LDL. Transepithelial electric resistance (TEER) and FITC-dextran permeability were measured. The effects of fenofibrate, its active metabolite fenofibric acid, and other peroxisome proliferator-activated receptor (PPARα) agonists (gemfibrozil, bezafibrate, and WY14643) were evaluated, with and without the PPARα antagonist GW6471 or the adenosine monophosphate-activated protein kinase (AMPK) inhibitor Compound C. Results: HOG-LDL induced concentration- and time-dependent barrier impairment, decreasing TEER and increasing dextran leakage, effects that were amplified by high glucose. Fenofibric acid, but not fenofibrate, gemfibrozil, bezafibrate, or WY14643, attenuated barrier impairment. This effect was reversed significantly by Compound C, but not by GW6471. Conclusions: Modified lipoproteins elicited outer BRB injury in an experimental model, which was reduced by fenofibric acid through a PPARα-independent, AMPK-mediated mechanism. These findings suggest a protective role of fenofibric acid on the outer BRB in diabetic retina.

[36] *Zanetti HR, Mendes EL, Gonçalves A et al.* **Effects of exercise training and statin on hemodynamic, biochemical, inflammatory and immune profile of people living with HIV: a randomized, double-blind, placebo-controlled trial**. J Sports Med Phys Fitness 2020; 60:1275-1282.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33124791
ABSTRACT
BACKGROUND: The aim of this study is to evaluate the effect of exercise training (ET) and statins on the hemodynamic, biochemical, inflammatory and immune profile of people living with HIV (PLHIV). METHODS: This was a randomized, double-blind, placebo-controlled clinical trial in which 83 PLHIV were assigned to either placebo (PL), statins (STA), placebo + ET

(PLET), or statins + ET (STAET) groups. Volunteers assigned to STA and STAET groups were administered 10 mg of rosuvastatin, whereas the PL and PLET groups were administered a placebo. The PLET and STAET groups performed ET three times a week. Before and after the 12-week follow-up, volunteers underwent blood collection to assess the biochemical, inflammatory, and immune profile. RESULTS: There were significant time x group interaction effects (P<0.05) for all variables except for diastolic blood pressure. The PLET and STAET groups had significantly (P<0.05) decreased systolic blood pressure, resting heart rate, fasting glucose, glycated hemoglobin, fasting insulin, homeostatic model assessment for insulin resistance, creatine kinase, lactate, and TNF-α levels, and increased adiponectin, CD4⁺, and CD8⁺ levels. There was also a significant group effect (P<0.05) for CK levels among the exercised (PLET and STAET) and STA groups. The latter had a significant increase in fasting glucose (P<0.05) and creatine kinase (P<0.05). CONCLUSIONS: ET improved the hemodynamic, biochemical, inflammatory, and immune profile of PLHIV and this effect was not dependent on the use of statins.

[37] *Dong J, He M, Li J et al.* **microRNA-483 ameliorates hypercholesterolemia by inhibiting PCSK9 production**. JCI insight 2020; 5.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33119548
ABSTRACT
Proprotein convertase subtilisin/kexin type 9 (PCSK9) affects cholesterol homeostasis by targeting hepatic LDL receptor (LDLR) for lysosomal degradation. Clinically, PCSK9 inhibitors effectively reduce LDL-cholesterol (LDL-C) levels and the incidence of cardiovascular events. Because microRNAs (miRs) are integral regulators of cholesterol homeostasis, we investigated the involvement of miR-483 in regulating LDL-C metabolism. Using in silico analysis, we predicted that miR-483-5p targets the 3'-UTR of PCSK9 mRNA. In HepG2 cells, miR-483-5p targeted the PCSK9 3'-UTR, leading to decreased PCSK9 protein and mRNA expression, increased LDLR expression, and enhanced LDL-C uptake. In hyperlipidemic mice and humans, serum levels of total cholesterol and LDL-C were inversely correlated with miR-483-5p levels. In mice, hepatic miR-483 overexpression increased LDLR levels by targeting Pcsk9, with a significant reduction in plasma total cholesterol and LDL-C levels. Mechanistically, the cholesterol-lowering effect of miR-483-5p was significant in mice receiving AAV8 PCSK9-3'-UTR but not Ldlr-knockout mice or mice receiving AAV8 PCSK9-3'-UTR (ΔBS) with the miR-483-5p targeting site deleted. Thus, exogenously administered miR-483 or similarly optimized compounds have potential to ameliorate hypercholesterolemia.

[38] *Hannon BA, Edwards CG, Thompson SV et al.* **Genetic Variants in Lipid Metabolism Pathways Interact with Diet to Influence Blood Lipid Concentrations in Adults with Overweight and Obesity**. Lifestyle genomics 2020; 13:155-163.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33105144
ABSTRACT
INTRODUCTION: The effect of various types of dietary fat on cardiometabolic health continues to be debated, due in part to the high heterogeneity of results following clinical trials investigating the effects of saturated (SFA) and unsaturated fat intake. This variability may be due to genetic differences. Individuals with obesity are at an increased risk for adverse cardiometabolic health and dyslipidemia, and often present with the combined phenotype of elevated triglyceride (TG) and decreased high-density lipoprotein (HDL) cholesterol

concentrations. Studying genetic variants relevant to lipid and lipoprotein metabolism can elucidate the mechanisms by which diet might interact with genotype to influence these phenotypes. The objective of this study was to determine relationships of genetic variation, dietary fat intake, and blood lipid concentrations in adults with overweight and obesity. METHODS: Genomic DNA, blood lipid concentrations (HDL and TG), and 7-day diet records were obtained from 101 adults (25-45 years of age) with overweight or obesity. Resting energy expenditure (REE) was measured using indirect calorimetry and used to determine implausible intakes using a modified Goldberg method (kilocalories/REE). Genetic variants included 23 single-nucleotide polymorphisms (SNPs) from 15 genes in lipid metabolism pathways. Variants were analyzed with dietary fat intake (total fat, SFA, monounsaturated fat [MUFA], and polyunsaturated fat [PUFA]) via regression analyses. All models were adjusted for age, sex, ancestry, visceral adipose tissue mass, and total kilocalorie intake. The Bonferroni correction was applied for multiple comparisons. RESULTS: Two interactions were detected for TG concentrations. Five gene-diet interactions were associated with HDL concentrations. There was a significant interaction detected between the rs5882 variant of cholesterol-esterase transfer protein (CETP) and MUFA intake to associate with TG concentrations (interaction p = 0.004, R2 = 0.306). Among carriers of the CETP-rs5882 major allele (G), TG concentrations were significantly lower in individuals consuming more than the median MUFA intake (31 g/day) than in those with an intake below the median. Total dietary fat intake interacted with the rs13702 polymorphism of lipoprotein lipase (LPL) to associate with HDL concentrations (interaction p = 0.041, R2 = 0.419), by which individuals with the risk allele (G) had significantly higher HDL concentrations when consuming a higher-fat diet (>92 g/day) than those with a lower-fat diet (56 ± 3 vs. 46 ± 2 mg/dL, p = 0.033). CONCLUSIONS: Interactions between dietary intake and genes in lipid metabolism pathways were found to be associated with blood lipid concentrations in adults with overweight and obesity. Fatty acid intake may not modulate blood lipid concentrations uniformly across all individuals. Additional research is needed to determine the biological causes of individual variability in response to dietary intake. Understanding the influence of nutrigenetic interactions on dyslipidemia can aid in the development and implementation of personalized dietary strategies to improve health.

[39] *Benincasa G, de Candia P, Costa D et al.* **Network Medicine Approach in Prevention and Personalized Treatment of Dyslipidemias**. Lipids 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33118184

ABSTRACT

Dyslipidemias can affect molecular networks underlying the metabolic homeostasis and vascular function leading to atherogenesis at early stages of development. Since disease-related proteins often interact with each other in functional modules, many advanced network-oriented algorithms were applied to patient-derived big data to identify the complex gene-environment interactions underlying the early pathophysiology of dyslipidemias and atherosclerosis. Both the proprotein convertase subtilisin/kexin type 7 (PCSK7) and collagen type 1 alpha 1 chain (COL1A1) genes arose from the application of TFfit and WGCNA algorithms, respectively, as potential useful therapeutic targets in prevention of dyslipidemias. Moreover, the Seed Connector algorithm (SCA) algorithm suggested a putative role of the neuropilin-1 (NRP1) protein as drug target, whereas a regression network analysis reported that niacin may provide benefits in mixed dyslipidemias. Dyslipidemias are highly heterogeneous at the clinical level; thus, it would be helpful to overcome traditional evidence-

based paradigm toward a personalized risk assessment and therapy. Network Medicine uses omics data, artificial intelligence (AI), imaging tools, and clinical information to design personalized therapy of dyslipidemias and atherosclerosis. Recently, a novel non-invasive AI-derived biomarker, named Fat Attenuation Index (FAI™) has been established to early detect clinical signs of atherosclerosis. Moreover, an integrated AI-radiomics approach can detect fibrosis and microvascular remodeling improving the customized risk assessment. Here, we offer a network-based roadmap ranging from novel molecular pathways to digital therapeutics which can improve personalized therapy of dyslipidemias.

[40] *Yan P, Zhao HX, Chen X*. **Suboptimal management of hypertriglyceridemia in the outpatient setting is associated with the recurrent pancreatitis: A retrospective cohort study**. Medicine (Baltimore) 2020; 99:e22887.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33120833
ABSTRACT
Hyperlipemia is a well-established etiology of acute pancreatitis. However, few data are available in the medical literature about the management of triglyceride levels in the outpatient setting in patients with hypertriglyceridemic acute pancreatitis (HTG-AP). We evaluated the blood triglyceride levels and followed the triglyceride management of patients with HTG-AP.This retrospective study enrolled patients with HTG-AP from January 2013 to March 2019 in the Affiliated Hospital of Southwest Medical of University. By reviewing the hospitalization records and the follow-up data, the clinical features, blood triglyceride levels, use of lipid-lowering medications and rate of blood triglyceride levels monitoring after hospital discharge were analyzed.A total of 133 patients (46 women, 87 men; median age at presentation 37.4 years) diagnosed with HTG-AP were enrolled in the study. Thirty-two patients (24.1%) presented with recurrent acute pancreatitis (RAP). Patients who had RAP were younger and had higher blood triglyceride levels than those with a single attack ($P < .05$). No difference in serum amylase levels, hospitalization duration or mortality rate were observed between non-recurrent acute pancreatitis and RAP patients. Lipid monitoring was only observed in 12.8% of patients and 10 patients (7.5%) took medications to control their blood triglyceride levels after hospital discharge. The follow-up of triglyceride levels in the outpatient setting were higher in RAP patients than in patients with non-recurrent acute pancreatitis ($P < .05$). Among the patients who measured their triglyceride levels after discharge, 83.3% of patients with RAP had at least 1 follow-up triglyceride level that was higher than 500 mg/dL, while no patients had an HTG-AP attack with a triglyceride level higher than 500 mg/dL.Triglyceride levels after hospital discharge higher than 500 mg/dL may be associated with an increased risk of relapse of clinical acute pancreatitis events. Inappropriate management for triglyceride control in the outpatient setting may be associated with an increased risk of relapse of clinical HTG-AP events.

[41] *Demler OV, Liu Y, Luttmann-Gibson H et al.* **One-Year Effects of Omega-3 Treatment on Fatty Acids, Oxylipins, and Related Bioactive Lipids and Their Associations with Clinical Lipid and Inflammatory Biomarkers: Findings from a Substudy of the Vitamin D and Omega-3 Trial (VITAL)**. Metabolites 2020; 10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33120862
ABSTRACT

Omega-3 (n-3) treatment may lower cardiovascular risk, yet its effects on the circulating lipidome and relation to cardiovascular risk biomarkers are unclear. We hypothesized that n-3 treatment is associated with favorable changes in downstream fatty acids (FAs), oxylipins, bioactive lipids, clinical lipid and inflammatory biomarkers. We examined these VITAL200, a nested substudy of 200 subjects balanced on demographics and treatment and randomly selected from the Vitamin D and Omega-3 Trial (VITAL). VITAL is a randomized double-blind trial of 840 mg/d eicosapentaenoic acid (EPA) + docosahexaenoic acid (DHA) vs. placebo among 25,871 individuals. Small polar bioactive lipid features, oxylipins and FAs from plasma and red blood cells were measured using three independent assaying techniques at baseline and one year. The Women's Health Study (WHS) was used for replication with dietary n-3 intake. Randomized n-3 treatment led to changes in 143 FAs, oxylipins and bioactive lipids (False Discovery Rate (FDR) < 0.05 in VITAL200, validated (p-values < 0.05)) in WHS with increases in 95 including EPA, DHA, n-3 docosapentaenoic acid (DPA-n3), and decreases in 48 including DPA-n6, dihomo gamma linolenic (DGLA), adrenic and arachidonic acids. N-3 related changes in the bioactive lipidome were heterogeneously associated with changes in clinical lipid and inflammatory biomarkers. N-3 treatment significantly modulates the bioactive lipidome, which may contribute to its clinical benefits.

[42] *Talha KA, Selina F, Nasir M et al.* **Systematic Review on Apolipoprotein E: A Strong Genetic Cause of Hemorrhagic Stroke**. Mymensingh medical journal : MMJ 2020; 29:1026-1032.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33116113
ABSTRACT
Stroke is one of the commonest causes of mortality among the world. Hemorrhagic stroke accounts nearly 15% of all the strokes. Different risk factors have been identified, of them hypertension, anti-coagulation therapy and previous history of ischemic strokes are significant. Regarding the genetic causes of intracerebral hemorrhage (ICH) monogenic causes play a small role. It was found that Apolipoprotein E (APOE) gene has a strong association with ICH. This is a 299 amino acids long protein located in chromosome 19. APOE has three alleles, they are epsilon 2, 3 and 4. Total 10 meta-analysis were reviewed in this article which involved 52,705 participants. When looking for the association, ∈2 and ∈4 showed positive and ∈3 showed negative association with ICH. Association of ∈4 (OR mean 1.77) was stronger than that of ∈2 (OR mean 1.71).

[43] *Zhang X, Bishawi M, Zhang G et al.* **Modeling early stage atherosclerosis in a primary human vascular microphysiological system**. Nature communications 2020; 11:5426.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33110060
ABSTRACT
Novel atherosclerosis models are needed to guide clinical therapy. Here, we report an in vitro model of early atherosclerosis by fabricating and perfusing multi-layer arteriole-scale human tissue-engineered blood vessels (TEBVs) by plastic compression. TEBVs maintain mechanical strength, vasoactivity, and nitric oxide (NO) production for at least 4 weeks. Perfusion of TEBVs at a physiological shear stress with enzyme-modified low-density-lipoprotein (eLDL) with or without TNFα promotes monocyte accumulation, reduces vasoactivity, alters NO production, which leads to endothelial cell activation, monocyte accumulation, foam cell formation and expression of pro-inflammatory cytokines. Removing eLDL leads to recovery of

vasoactivity, but not loss of foam cells or recovery of permeability, while pretreatment with lovastatin or the P2Y(11) inhibitor NF157 reduces monocyte accumulation and blocks foam cell formation. Perfusion with blood leads to increased monocyte adhesion. This atherosclerosis model can identify the role of drugs on specific vascular functions that cannot be assessed in vivo.

[44] *Smith CA*. **Fibrate Use and Patients with Chronic Kidney Disease**. Nephrol Nurs J 2020; 47:475-477.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33107720
ABSTRACT

[45] *Sayyah M, Shirbandi K, Rahim F, Ganji R*. **Statin for Migraine Headache: Is It Worthwhile?** Neurol India 2020; 68:1003-1007.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33109841
ABSTRACT
Migraine is a severe primary headache disorder that affects about 12% of the population, and it often occurs along with nausea, vomiting, and extreme sensitivity to light and sound. For patients with migraine, beta-blockers, antidepressants, anticonvulsants, are given as the first line of preventive treatment; alternatives include calcium channel blockers. Not only statins prevent the synthesis of cholesterol biosynthesis but also they have a pleiotropic effect such as antiinflammatory effects, antioxidant property, antiproliferative and immunomodulatory effects, the stability of plaque, normalization of sympathetic outflow, and inhibit of platelet aggregation. Here, we should focus on the evidence that works on the effect of the statins on migraine headaches, especially in patients who do not respond to first-line prevention treatments. The hypothesis may show that statins could be effective in the treatment of patients with migraine. Taken together, some epidemiologic, clinical, and experimental evidence suggest that statin may be a novel and promising candidate. For future treatment or prophylaxis of migraine, we hope that the use of this drug as cholesterol and triglycerides(blood lipids) leads to rebate drugs, as well as to reduce migraine headaches episodes agent to enhance the role of this drug in cure or prevent migraine attacks or recurrence, and finally to improve the patient's quality of life.

[46] *Chen C, Wu H, Kong D et al.* **Transcriptome sequencing analysis reveals unique and shared antitumor effects of three statins in pancreatic cancer**. Oncology reports 2020; 44:2569-2580.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33125137
ABSTRACT
Statins, a class of commonly prescribed cholesterol-lowering medications, have been revealed to influence the risk of multiple types of cancer. However, the antitumor effects of statins on pancreatic cancer and their differential efficacy among a variety of statins are not currently well-defined. The aim of the present study was therefore to identify and compare the genes and related biological pathways that were affected by each individual statin on pancreatic cancer. Two human pancreatic cancer cell lines, MiaPaCa2 and PANC1, were exposed to three statins, lovastatin, fluvastatin and simvastatin. The inhibitory effect of statins on pancreatic cancer cell proliferation was first validated. Next, RNA-seq analysis was used to determine the gene expression alterations in either low (2 μM) or high (20 μM) statin

concentration-treated cancer cells. Marked differences in gene transcription profiles of both pancreatic cancer cell lines exposed to high concentration statins were observed. Notably, the high concentration statins significantly suppressed core-gene CCNA2-associated cell cycle and DNA replication pathways and upregulated genes involved in ribosome and autophagy pathways. However, the low concentration statin-induced gene expression alterations were only detected in MiaPaCa2 cells. In conclusion, a marked difference in the intra and inter cell-type performance of pancreatic cancer cells exposed to a variety of statins at low or high concentrations was reported herein, which may provide insights for the potential clinical use of statins in future pancreatic cancer therapeutics.

[47] *Yu B, He W, He C et al.* **Low-Molecular-Weight Heparin Combined With Insulin Versus Insulin Alone in the Treatment of Hypertriglyceridemic Pancreatitis (LIHTGP Trial): Study Protocol for a Multicenter, Prospective, Single-Blind, Randomized Controlled Trial**. Pancreas 2020; 49:1383-1387.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33122529
ABSTRACT
OBJECTIVE: Currently, insulin and/or heparin/low-molecular-weight heparin (LMWH) serve as an early lipid-lowering treatment for hypertriglyceridemic pancreatitis (HTGP). However, whether the clinical prognosis of combining LMWH with insulin is superior to using insulin alone remains unknown. This trial will compare the clinical outcomes of LMWH with insulin and an insulin regimen for emergency lipid-lowering treatment in HTGP patients. METHODS: In total, 476 eligible participants will be recruited from 18 hospitals throughout China. Participants in the LMWH group will receive LMWH combined with insulin, whereas insulin alone will be administered to those in the insulin group. The patients will be followed up at 3 and 6 months after discharge. Adverse reactions will be evaluated by the safety monitoring committee. Safety outcomes and adverse events will also be recorded. RESULTS: The study is registered in the Chinese Clinical Trial Registry (No: ChiCTR1900023640). Recruitment will begin in August 2019 and will be completed in December 2021 (http://www.chictr.org.cn/index.aspx). No data are available now. CONCLUSIONS: The trial will investigate the efficacy of using LMWH combined with insulin as an emergency lipid-lowering treatment in reducing new organ failure, mortality, hospital stays, and expenses compared using with insulin alone for patients with HTGP.

[48] *Robinson JG, Jayanna MB, Bairey Merz CN, Stone NJ*. **Clinical implications of the log linear association between LDL-C lowering and cardiovascular risk reduction: Greatest benefits when LDL-C >100 mg/dl**. PloS one 2020; 15:e0240166.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33119602
ABSTRACT
BACKGROUND: The log linear association between on-treatment LDL-C levels and ASCVD events is amplified in higher risk patient subgroups of statin versus placebo trials. OBJECTIVES: Update previous systematic review to evaluate how the log linear association influences the magnitude of cardiovascular risk reduction from intensifying LDL-C lowering therapy. METHODS: MEDLINE/PubMED, Clinical trials.gov, and author files were searched from 1/1/2005 through 10/30/2019 for subgroup analyses of cardiovascular outcomes trials of moderate versus high intensity statin, ezetimibe, and PCSK9 mAbs with an ASCVD endpoint (nonfatal myocardial infarction or stroke, cardiovascular death). Annualized ASCVD event

rates were used to extrapolate 5-year ASCVD risk for each treatment group reported in subgroup analyses, which were grouped into a priori risk groups according to annualized placebo/control rates of ≥4%, 3-3.9%, or <3% ASCVD risk. Data were pooled using a random-effects model. Weighted least-squares regression was used to fit linear and log-linear models. RESULTS: Systematic review identified 96 treatment subgroups from 2 trials of moderate versus high intensity statin, 2 trials of a PCSK9 mAb versus placebo, and 1 trial of ezetimibe versus placebo. A log linear association between on-treatment LDL-C and ASCVD risk represents the association between on-treatment LDL-C levels and ASCVD event rates, especially in higher risk subgroups. Greater relative and absolute cardiovascular risk reductions from LDL-C lowering were observed when baseline LDL-C was >100 mg/dl and in extremely high risk ASCVD patient groups. CONCLUSIONS: Greater cardiovascular and mortality risk reduction benefits from intensifying LDL-C lowering therapy may be expected in those with LDL-C ≥100 mg/dl, or in extremely high risk patient groups. When baseline LDL-C <100 mg/dl, the log linear association between LDL-C and event rates suggests that treatment options other than further LDL-C lowering should also be considered for optimal risk reduction.

[49] *Gołuchowska A, Lipert A, Grzegorczyk J et al.* **Changes in lipid and apolipoprotein levels in response to 8-week cardiac rehabilitation in men with coronary artery disease**. Polski merkuriusz lekarski : organ Polskiego Towarzystwa Lekarskiego 2020; 48:302-306.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33130787

ABSTRACT

Concentrations of selected lipoproteins are currently useful cardiovascular risk assessment indicators, especially in monitoring lipid-lowering therapy. AIM: The aim was to evaluate the influence of 8-week mid-term CR on apolipoproteins: A-I, B, E and VLDL in CAD patients in relation to conventional lipid profile and prior coronary intervention: PCI or CABG. MATERIALS AND METHODS: 93 male patients admitted to CR after PCI or CABG. At baseline and after CR, conventional lipid profile parameters and VLDL concentrations were evaluated. Apolipoproteins: A-I, B, E were also determined. Basic anthropometric indicators and measurements of hemodynamic and exercise tolerance at rest and peak workload in exercise testing (HR, sBP, dBP, DP, W) were measured. RESULTS: After CR, depending on revasculazation intervention, no changes in HDL-C, LDL-C, TG and VLDL values were observed (p>0.05). Reduction in apoA-I was noted in PCI group (p=0.0254). No statistically significant changes in apoB and apoE were found in groups. Significant increase in apo B/apo A-I index was observed only in PCI group (p=0.0329). PCI and CABG patients did not differ in hemodynamic and exercise tolerance parameters, except sBP in rest and dBP at peak workload in exercise testing (p=0.014 and p=0.031). Regardless on type of intervention, there was observed statistically significant increase in Wpeak (p=0,0000 in both groups) and DPpeak (p=0.0000 in PCI-patients and p=0.0003 in CABGpatients) after CR. CONCLUSIONS: CR has various effects on lipid concentrations. Indicators of conventional lipid profile and selected apolipoproteins are not optimal parameters allowing assessment of effectiveness of CR program in such a short time, this role is well fullfilled by the hemodynamic and physical exercise indices. Apo B/apo A-I ratio value suggests an increasing risk of IHD complications, especially in post- PCI group. CR program requires intensification of lipid-reducing therapy and education on lifestyle modification.

[50] *Chen CL, Liu XC, Liu L et al.* **U-Shaped Association of High-Density Lipoprotein Cholesterol with All-Cause and Cardiovascular Mortality in Hypertensive Population**. Risk Manag Healthc Policy 2020; 13:2013-2025.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33116982
ABSTRACT
PURPOSE: Whether the paradox of high-density lipoprotein cholesterol (HDL-C) and elevated mortality risk extends to hypertensive patients is unclear. We aimed to investigate the association between HDL-C and all-cause and cardiovascular disease mortality in adults with hypertension. METHODS: In the National Health and Nutrition Examination Surveys, 11,497 hypertensive participants aged ≥18years old and examined at baseline between 1999 and 2014 were followed up until December 2015. We categorized the HDL-C concentration as ≤30, 31-40, 41-50, 51-60 (reference), 61-70, >70 mg/dL and examined their associations with all-cause and cardiovascular mortality, respectively. Multivariate Cox regression was used to calculated hazard ratio (HR) and 95% confidence interval (CI) for mortality risk. RESULTS: During follow-up (median: 9.2 ± 3.8 years), 3012 deaths and 713 cardiovascular deaths were observed. In the restrictive cubic curves, associations of HDL-C levels and all-cause and cardiovascular mortality were detected to be U-shaped. After multivariable adjustment, HRs for all-cause mortality were for the lowest HDL-C concentration (≤30 mg/dL) 1.29 (95% CI, 1.07-1.56) and the highest (>70 mg/dL) 1.20 (1.06-1.37), comparing with the reference group. For cardiovascular mortality, HRs were 1.31 (0.83-1.48) and 1.09 (0.83-1.43), respectively. Similar results were obtained in subgroups stratified by age, gender, race, and taking lipid-lowering drugs. The lowest all-cause mortality risk was observed at HDL-C 66 mg/dL (concentration) and 51-60 mg/dL (range). CONCLUSION: Both lower and higher HDL-C concentration appeared to be associated with higher mortality in hypertensive population. Further investigation is warranted to clarify the underlying mechanisms.

[51] *Santiago-Raber ML, Montecucco F, Vuilleumier N et al.* **Atherosclerotic plaque vulnerability is increased in mouse model of lupus**. Scientific reports 2020; 10:18324.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33110193
ABSTRACT
Anti-apolipoprotein A-1 (anti-apoA-1 IgG) and anti-double stranded DNA (anti-dsDNA IgG) autoantibodies have been described as mediators of atherogenesis in mice and humans. In the present study, we aim to investigate the association between atherosclerotic parameters, autoantibodies and plaque vulnerability in the context of systemic lupus erythematosus (SLE). We therefore bred a lupus prone-mouse model (Nba2.Yaa mice) with Apoe(-/-) mice resulting in Apoe(-/-)Nba2.Yaa mice spontaneously producing anti-apoA-1 IgG antibodies. Although Apoe(-/-)Nba2.Yaa and Apoe(-/-) mice subject to a high cholesterol diet displayed similar atherosclerosis lesions size in aortic roots and abdominal aorta, the levels of macrophage and neutrophil infiltration, collagen, MMP-8 and MMP-9 and pro-MMP-9 expression in Apoe(-/-)Nba2.Yaa mice indicated features of atherosclerotic plaque vulnerability. Even though Apoe(-/-)Nba2.Yaa mice and Apoe(-/-) mice had similar lipid levels, Apoe(-/-)Nba2.Yaa mice showed higher anti-apoA-1 and anti-dsDNA IgG levels. Apoe(-/-)Nba2.Yaa mice displayed a reduction of the size of the kidney, splenomegaly and lymph nodes (LN) hypertrophy. In addition, anti-apoA-1 and anti-dsDNA IgG increased also in relation with mRNA levels of GATA3, IL-4, Bcl-6 and CD20 in the spleen and aortic arch of Apoe(-/-)Nba2.Yaa mice. Our data show that although atherosclerosis-lupus-prone Apoe(-/-)Nba2.Yaa mice did not exhibit exacerbated

atherosclerotic lesion size, they did show features of atherosclerotic plaque destabilization in correlation with the increase of pro-atherogenic autoantibodies.

[52] **Correction to: PCSK9 (Proprotein Convertase Subtilisin-Kexin Type 9) Inhibition and Stroke Prevention: Another Step Forward**. Stroke 2020; 51:e348.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33104492
ABSTRACT

[53] *Spence JD, Azarpazhooh MR, Larsson SC et al.* **Stroke Prevention in Older Adults: Recent Advances**. Stroke 2020; 51:3770-3777.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33121384
ABSTRACT
The risks of stroke and dementia increase steeply with age, and both are preventable. At present, the best way to preserve cognitive function is to prevent stroke. Therapeutic nihilism based on age is common and unwarranted. We address recent advances in stroke prevention that could contribute greatly to prevention of stroke and dementia at a time when the aging of the population threatens to markedly increase the incidence of both. Issues discussed: (1) old patients benefit even more from lipid-lowering therapy than do younger patients; (2) patients with stiff arteries are at risk from a target systolic blood pressure <120 mm Hg; (3) the interaction of the intestinal microbiome, age, and renal function has important dietary implications for older adults; (4) anticoagulation with direct-acting oral anticoagulants should be prescribed more to old patients with atrial fibrillation; (5) B vitamins to lower homocysteine prevent stroke; and (6) most old patients in whom intervention is warranted for carotid stenosis would benefit more from endarterectomy than from stenting. An 80-year-old person has much to lose from a stroke and should not have effective therapy withheld on account of age. Lipid-lowering therapy, a more plant-based diet, appropriate anticoagulation or antiplatelet therapy, appropriate blood pressure control, B vitamins to lower homocysteine, and judicious intervention for carotid stenosis could do much to reduce the growing burden of stroke and dementia.

[54] *Li L, Pan Y, Wang M et al.* **Trends and predictors of myocardial infarction or vascular death after ischaemic stroke or TIA in China, 2007-2018: insights from China National Stroke Registries**. Stroke and vascular neurology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33127855
ABSTRACT
BACKGROUND: Although stroke management, primary and secondary preventions have been improved in China last decades, the trends and predictors of major vascular events after ischaemic stroke or transient ischaemic attack (TIA) at national scale are less known. METHODS: Data were obtained from the three phases of China National Stroke Registry (CNSR), including CNSR-Ⅰ (years 2007-2008), CNSR-Ⅱ (years 2012-2013) and CNSR-III (years 2015-2018). For comparison, patients who were diagnosed as ischaemic stroke or TIA were included. Kaplan-Meier estimates of myocardial infarction (MI) or vascular death were calculated at 1 year. Independent predictors were further assessed with a Cox proportional hazards regression. RESULTS: From 2007 to 2018, a total of 50 284 patients with ischaemic stroke or TIA were enrolled in this study. A declining trend was found in 1-year MI or vascular death (p for trend <0.001), while recurrent stroke depicted a U-shape curve with a nadir in

2012-2013 cohort. A similar trend was also observed in patients who were admitted to 26 hospitals in all three CNSRs. In 2015-2018 cohort, only 251 (1.7%; 95% CI 1.5% to 1.9%) MI or vascular death had occurred at 1 year. Older age, previous stroke or TIA, history of coronary artery disease and the National Institutes of Health Stroke Scale >6 were associated with both an increased risk of MI or vascular death and recurrent stroke. While early antiplatelet therapy and lipid-lowering agents at discharge predicted a reduced risk. CONCLUSION: A declining trend and current low incidence of MI or vascular death, rather than recurrent stroke, after ischaemic stroke or TIA were observed in China. Traditional factors were found as independent predictors. These findings suggested there is still much room to improve for stroke management.

[55] *Ghati N, Roy A, Bhatnagar S et al.* **Atorvastatin and Aspirin as Adjuvant Therapy in Patients with SARS-CoV-2 Infection: A structured summary of a study protocol for a randomised controlled trial**. Trials 2020; 21:902.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33126910
ABSTRACT
OBJECTIVES: To assess the impact of adding statin (atorvastatin) and/or aspirin on clinical deterioration in patients infected with SARS-CoV-2 who require hospitalisation. The safety of these drugs in COVID-19 patients will also be evaluated. TRIAL DESIGN: This is a single-centre, prospective, four-arm parallel design, open-label, randomized control trial. PARTICIPANTS: The study will be conducted at National Cancer Institute (NCI), Jhajjar, Haryana, which is a part of All India Institute of Medical Sciences (AIIMS), New Delhi, and has been converted into a dedicated COVID-19 management centre since the outbreak of the pandemic. All RT-PCR confirmed cases of SARS-CoV-2 infection with age ≥ 40 years and < 75 years requiring hospital admission (patients with WHO clinical improvement ordinal score 3 to 5) will be included in the trial. Written informed consent will be taken for all recruited patients. Patients with a critical illness (WHO clinical improvement ordinal score > 5), documented significant liver disease/dysfunction (aspartate transaminase [AST] / alanine aminotransferase [ALT] > 240), myopathy and rhabdomyolysis (creatine phosphokinase [CPK] > 5x normal), allergy or intolerance to statins or aspirin, prior statin or aspirin use within 30 days, history of active gastrointestinal bleeding in past three months, coagulopathy, thrombocytopenia (platelet count < 100000/ dl), pregnancy, active breastfeeding, or inability to take oral or nasogastric medications will be excluded. Patients refusing to give written consent and taking drugs that are known to have a significant drug interaction with statin or aspirin [including cyclosporine, HIV protease inhibitors, hepatitis C protease inhibitor, telaprevir, fibric acid derivatives (gemfibrozil), niacin, azole antifungals (itraconazole, ketoconazole), clarithromycin and colchicine] will also be excluded from the trial. INTERVENTION AND COMPARATOR: In this study, the benefit and safety of atorvastatin (statin) and/or aspirin as adjuvant therapy will be compared with the control group receiving usual care for management of COVID-19. Atorvastatin will be prescribed as 40 mg oral tablets once daily for ten days or until discharge, whichever is earlier. The dose of aspirin will be 75 mg once daily for ten days or until discharge, whichever is earlier. All other therapies will be administered according to the institute's COVID-19 treatment protocol and the treating physician's clinical judgment. MAIN OUTCOMES: All study participants will be prospectively followed up for ten days or until hospital discharge, whichever is longer for outcomes. The primary outcome will be clinical deterioration characterized by progression to WHO clinical improvement ordinal score ≥ 6 (i.e.,

endotracheal intubation, non-invasive mechanical ventilation, pressor agents, renal replacement therapy, ECMO requirement, and mortality). The secondary outcomes will be change in serum inflammatory markers (C-reactive protein and Interleukin-6), Troponin I, and creatine phosphokinase (CPK) from time zero to 5th day of study enrolment or 7th day after symptom onset, whichever is later. Other clinical outcomes that will be assessed include progression to Acute Respiratory Distress Syndrome (ARDS), shock, ICU admission, length of ICU admission, length of hospital admission, and in-hospital mortality. Adverse drug effects like myalgia, myopathy, rhabdomyolysis, hepatotoxicity, and bleeding will also be examined in the trial to assess the safety of the interventions. RANDOMISATION: The study will use a four-arm parallel-group design. A computer-generated permuted block randomization with mixed block size will be used to randomize the participants in a 1:1:1:1 ratio to group A (atorvastatin with conventional therapy), group B (aspirin with conventional therapy), group C (aspirin + atorvastatin with conventional therapy), and group D (control; only conventional therapy). BLINDING (MASKING): The study will be an open-label trial. NUMBERS TO BE RANDOMISED (SAMPLE SIZE): As there is no existing study that has evaluated the role of aspirin and atorvastatin in COVID-19 patients, formal sample size calculation has not been done. Patients satisfying the inclusion and exclusion criteria will be recruited during six months of study period. Once the first 200 patients are included in each arm (i.e., total 800 patients), the final sample size calculation will be done on the basis of the interim analysis of the collected data. TRIAL STATUS: The institutional ethical committee has approved the study protocol (Protocol version 3.0 [June 2020]). Participant recruitment starting date: 28(th) July 2020 Participant recruitment ending date: 27(th) January 2021 Trial duration: 6 months TRIAL REGISTRATION: The trial has been prospectively registered in Clinical Trial Registry - India (ICMR- NIMS): Reference no. CTRI/2020/07/026791 (registered on 25 July 2020)]. FULL PROTOCOL: The full protocol is attached as an additional file, accessible from the Trials website (Additional file 1). In the interest of expediting dissemination of this material, the familiar formatting has been eliminated; this Letter serves as a summary of the key elements of the full protocol.

[56] *Duprez DA, Handelsman Y, Koren M*. **Cardiovascular Outcomes and Proprotein Convertase Subtilisin/Kexin Type 9 Inhibitors: Current Data and Future Prospects**. Vascular health and risk management 2020; 16:403-418.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33116551

ABSTRACT

Cardiovascular (CV) disease remains the leading cause of morbidity and mortality worldwide and poses an ongoing challenge with the aging population. Elevated low-density lipoprotein cholesterol (LDL-C) is an established risk factor for atherosclerotic cardiovascular disease (ASCVD), and the expert consensus is the use of statin therapy (if tolerated) as first line for LDL-C reduction. However, patients with ASCVD may experience recurrent ischemic events despite receiving maximally tolerated statin therapy, including those whose on-treatment LDL-C remains ≥70 mg/dL, patients with familial hypercholesterolemia, high-risk subgroups with comorbidities such as diabetes mellitus, and those who have an intolerance to statin therapy. Optimal therapeutic strategies for this unmet need should deploy aggressive lipid lowering to minimize the contribution of dyslipidemia to their CV risk, particularly for very high-risk populations with additional risk factors beyond hypercholesterolemia and established ASCVD. To understand the current clinical climate and guidelines regarding ASCVD, we primarily

searched PubMed for articles published in English regarding lipid-lowering therapies and CV risk reduction, including emerging therapies, and CV outcomes trials with proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors. This review discusses the findings of recent clinical trial evidence for CV risk reduction with cholesterol-lowering therapies, with a focus on CV outcomes trials with PCSK9 inhibitors, and considers the impact of the study results for secondary prevention and future strategies in patients with hypercholesterolemia and CV risk despite maximally tolerated statin therapy.