[1] *Mohamud AY, Griffith B, Rehman M et al.* **Intraluminal Carotid Artery Thrombus in COVID-19: Another Danger of Cytokine Storm?** AJNR. American journal of neuroradiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32616585
ABSTRACT
Coronavirus disease 2019 (COVID-19) is associated with a severe inflammatory response. Inflammation affects atherosclerotic plaque vulnerability and promotes a thrombogenic environment. We report a series of 6 patients with COVID-19 with acute ischemic stroke due to intraluminal carotid artery thrombus presenting during an 8-day period. Six patients were included (5 men) with a mean age of 65.8 years (range, 55-78 years). COVID-19 was diagnosed by detection of Severe Acute Respiratory Syndrome coronavirus 2 in 5 patients and was presumed due to typical clinical and imaging findings in 1 patient. All patients had vascular risk factors including diabetes (83%), hyperlipidemia (100%), and smoking (17%). Four patients presented with large infarcts with initial NIHSS scores of 24-30. During their hospitalization, all patients had elevated D-dimer and C-reactive protein levels, 5 patients had elevated lactate dehydrogenase and ferritin levels, 3 had elevated interleukin-6 levels, and 2 had elevated troponin levels. Inflammation related to COVID-19 may result in rupture of vulnerable atherosclerotic plaques, resulting in thrombosis and acute ischemic stroke.

[2] *Mendoza M, Ferrer-Oliveras R, Bonacina E et al.* **Evaluating the Effect of Pravastatin in Early-Onset Fetal Growth Restriction: A Nonrandomized and Historically Controlled Pilot Study**. Am J Perinatol 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32615618
ABSTRACT
OBJECTIVE: This study aimed to analyze the effect of pravastatin on angiogenic factors, feto-maternal Doppler findings and pregnancy outcomes in women with early-onset fetal growth restriction (FGR) treated with pravastatin compared with nontreated controls. STUDY DESIGN: This was a pilot study conducted between March 2016 and September 2017. Women with single pregnancies and FGR diagnosed at ≤ 28 weeks of gestation were offered 40 mg of pravastatin daily. Doppler progression, soluble fms-like tyrosine kinase 1 (sFlt-1)/placental growth factor (PlGF) values, and pregnancy outcomes were assessed and compared with consecutive historical controls. Controls were matched to treated women for gestational age, maternal characteristics, maternal and obstetric history, Doppler severity classification, and angiogenic factors at diagnosis. The sFlt-1/PlGF was measured in maternal serum at two different times: before pravastatin was started (ratio M0) and during pravastatin treatment (ratio M1). Doppler severity was classified into four categories: normal, mild, moderate, and severe. RESULTS: A total of 38 women were enrolled in this study. No differences were observed in baseline characteristics between groups. However, when compared with the ratio M0, M1 was increased by a median (interquartile range) of 67.0 (-34.8 to 197.3) in the control group but decreased by a median (interquartile range) of -10.1 (-53.1 to -0.07) in the pravastatin treated group ($p < 0.001$). No significant differences were observed in Doppler progression throughout pregnancy. Median interval from diagnosis to delivery was extended by 16.5 days, the median newborn birthweight was increased from 1,040 to 1,300 g, and the number of women with preeclampsia decreased from 9 (47.4%) to 6 (31.6%) in treated women; however, these trends were not statistically significant. CONCLUSION: In women with early-onset FGR, treatment with pravastatin 40 mg daily was associated with significant

improvement in the angiogenic profile. Additionally, median pregnancy duration and median birthweight increased and the incidence of PE was reduced in treated women. Nevertheless, since this pilot study was underpowered, none of these differences were statistically significant. KEY POINTS: · Pravastatin improves sFlt-1/PlGF in FGR.. · Pregnancy duration tended to be greater in treated women.. · Birthweight tended to be greater in treated women..

[3] *Zeng Q, Rong Y, Li D et al.* **Identification of serum biomarker in Acute Aortic Dissection by global and targeted Metabolomics**. Annals of vascular surgery 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32599111
ABSTRACT
OBJECTIVE: Acute aortic dissection (AAD) is the most devastating aortic pathology and the incidence is increasing worldwide. However, the occurrence and development of AAD are unpredictable. A thorough understanding of the serum metabolic landscape through metabolomic analysis may help identify new biomarkers for AAD, and offer new insights into its prevention and evaluation. METHODS: 19 patients with Stanford Type A aortic dissection and 20 healthy individuals were enrolled in this study. We use global and targeted mass spectrometry-based metabolomics to investigate the serum metabolomics profiles and the data were analyzed by principal component analysis and orthogonal partial least squares discriminant analysis. RESULTS: Initial untargeted metabolomics analysis revealed significant changes of lipids and polar metabolites in patients with AAD. Alterations of the phosphatidylcholine metabolic pathway were further observed by targeted metabolomics. Trimethylamine N-Oxide (TMAO) levels were obviously increased in patients with AAD compared with controls ($p<0.005$), while the levels of carnitine ($p<0.005$), choline and betaine ($p<0.05$) were decreased. Furthermore, TMAO levels was associated with disease severity in AAD, and correlated positively with CRP levels ($r=0.537$, $P=0.018$), IL-6 levels ($r=0.546$, $P=0.016$), D-dimer levels ($r=0.694$, $P=0.001$) and maximum aortic diameter on admission ($r=0.748$, $P=0.002$). CONCLUSIONS: Patients with AAD showed a predominant and consistent change of metabolites levels, especially the compounds in the phosphatidylcholine metabolic pathway. TMAO could potentially serve as a biomarker for the auxiliary diagnosis and evaluation of AAD.

[4] *Safaeian L, Mirian M, Bahrizadeh S*. **Evolocumab, a PCSK9 inhibitor, protects human endothelial cells against H(2)O(2)-induced oxidative stress**. Archives of physiology and biochemistry 2020:1-6.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32619370
ABSTRACT
Context: Recent surveys have shown an association between proprotein convertase subtilisin/kexin type 9 (PCSK9) and oxidative stress.Objective: In this investigation, the effect of evolocumab an anti-PCSK9 antibody was assessed against oxidative damage caused by hydrogen peroxide (H(2)O(2)) in human umbilical vein endothelial cells (HUVEC).Material and methods: Viability of HUVEC was measured by MTT assay. Hydroperoxides and malondialdehyde (MDA) levels, and ferric reducing antioxidant power (FRAP) were detected in HUVEC that pre-treated with evolocumab and, then exposed to H(2)O(2).Results: Evolocumab significantly prevented the cytotoxicity induced by H(2)O(2) at the concentrations of 5-100 µg/ml. Pre-treatment of HUVEC with evolocumab reduced hydroperoxides and MDA levels and also increased FRAP value in intra- and extra-cellular mediums compared with H(2)O(2)

stimulated cells at different concentration ranges.Conclusion: This study displayed anti-oxidative and cytoprotective activities of evolocumab against oxidative damage caused by H(2)O(2) in endothelial cells.

[5] *Ruuth M, Äikäs L, Tigistu-Sahle F et al.* **Plant Stanol Esters Reduce LDL (Low-Density Lipoprotein) Aggregation by Altering LDL Surface Lipids: The BLOOD FLOW Randomized Intervention Study**. Arteriosclerosis, thrombosis, and vascular biology 2020:Atvbaha120314329.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32611242
ABSTRACT
OBJECTIVE: Plant stanol ester supplementation (2-3 g plant stanols/d) reduces plasma LDL (low-density lipoprotein) cholesterol concentration by 9% to 12% and is, therefore, recommended as part of prevention and treatment of atherosclerotic cardiovascular disease. In addition to plasma LDL-cholesterol concentration, also qualitative properties of LDL particles can influence atherogenesis. However, the effect of plant stanol ester consumption on the proatherogenic properties of LDL has not been studied. Approach and Results: Study subjects (n=90) were randomized to consume either a plant stanol ester-enriched spread (3.0 g plant stanols/d) or the same spread without added plant stanol esters for 6 months. Blood samples were taken at baseline and after the intervention. The aggregation susceptibility of LDL particles was analyzed by inducing aggregation of isolated LDL and following aggregate formation. LDL lipidome was determined by mass spectrometry. Binding of serum lipoproteins to proteoglycans was measured using a microtiter well-based assay. LDL aggregation susceptibility was decreased in the plant stanol ester group, and the median aggregate size after incubation for 2 hours decreased from 1490 to 620 nm, P=0.001. Plant stanol ester-induced decrease in LDL aggregation was more extensive in participants having body mass index<25 kg/m(2). Decreased LDL aggregation susceptibility was associated with decreased proportion of LDL-sphingomyelins and increased proportion of LDL-triacylglycerols. LDL binding to proteoglycans was decreased in the plant stanol ester group, the decrease depending on decreased serum LDL-cholesterol concentration. CONCLUSIONS: Consumption of plant stanol esters decreases the aggregation susceptibility of LDL particles by modifying LDL lipidome. The resulting improvement of LDL quality may be beneficial for cardiovascular health. REGISTRATION: URL: https://www.clinicaltrials.gov. Unique identifier: NCT01315964.

[6] *Fotso Soh J, Beaulieu S, Trepiccione F et al.* **A double-blind, randomized, placebo-controlled pilot trial of atorvastatin for nephrogenic diabetes insipidus in lithium users**. Bipolar Disord 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32621644
ABSTRACT
OBJECTIVE: Lithium remains an important treatment for mood disorders but is associated with kidney disease. Nephrogenic diabetes insipidus (NDI) is associated with up to 3-fold risk of incident chronic kidney disease among lithium users. There are limited randomized controlled trials (RCT) for treatments of lithium-induced NDI, and existing therapies can be poorly tolerated. Therefore, novel treatments are needed for lithium-induced NDI. METHOD: We conducted a 12-week double-blind pilot RCT to assess the feasibility and efficacy of 20 mg/d atorvastatin vs placebo in the treatment of NDI in chronic lithium users. Patients, recruited between September 2017 and October 2018, were aged 18 to 85, currently on a stable dose of

lithium, and determined to have NDI. RESULTS: Urinary osmolality (UOsm) at 12 weeks adjusted for baseline was not statistically different between groups (+39.6 mOsm/kg [95% CI, -35.3, 114.5] in atorvastatin compared to placebo groups). Secondary outcomes of fluid intake and aquaporin-2 excretions at 12 weeks adjusted for baseline were -0.13 L [95% CI, -0.54, 0.28] and 98.68 [95% CI, -190.34, 387.70], respectively. A moderate effect size was observed for improvements in baseline UOsm by ≥100 mOsm/kg at 12 weeks in patients who received atorvastatin compared to placebo (38.45% (10/26) vs 22.58% (7/31); Cohen's d = 0.66). CONCLUSION: Among lithium users with NDI, atorvastatin 20 mg/d did not significantly improve urinary osmolality compared to placebo over a 12-week period. Larger confirmatory trials with longer follow-up periods may help to further assess the effects of statins on NDI, especially within patients with more severe NDI.

[7] *Curtis HJ, Walker AJ, MacKenna B et al.* **Prescription of suboptimal statin treatment regimens: a retrospective cohort study of trends and variation in English primary care**. Br J Gen Pract 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32601055
ABSTRACT
BACKGROUND: Since 2014 English national guidance recommends 'high-intensity' statins, reducing low-density lipoprotein (LDL) cholesterol by ≥40%. AIM: To describe trends and variation in low-/medium-intensity statin prescribing and assess the feasibility of rapid prescribing behaviour change. DESIGN AND SETTING: A retrospective cohort study using OpenPrescribing data from all 8142 standard NHS general practices in England from August 2010 to March 2019. METHOD: Statins were categorised as high- or low-/medium-intensity using two different thresholds, and the proportion prescribed below these thresholds was calculated. The authors plotted trends and geographical variation, carried out mixed-effects logistic regression to identify practice characteristics associated with breaching of guidance, and used indicator saturation to identify sudden prescribing changes. RESULTS: The proportion of statins prescribed below the recommended 40% LDL-lowering threshold has decreased gradually from 80% in 2011/2012 to 45% in 2019; the proportion below a pragmatic 37% threshold decreased from 30% to 18% in 2019. Guidance from 2014 had minimal impact on trends. Wide variation was found between practices (interdecile ranges 20% to 85% and 10% to 30% respectively in 2018). Regression identified no strong associations with breaching of guidance. Indicator saturation identified several practices exhibiting sudden changes towards greater guideline compliance. CONCLUSION: Breaches of guidance on choice of statin remain common, with substantial variation between practices. Some have implemented rapid change, indicating the feasibility of rapid prescribing behaviour change. This article discusses the potential for a national strategic approach, using data and evidence to optimise care, including targeted education alongside audit and feedback to outliers through services such as OpenPrescribing.

[8] *Fan W, Tong C, Wong ND*. **LEADER Trial Eligibility and Preventable Cardiovascular Events in US Adults with Diabetes: the National Health and Nutrition Examination Surveys 2007-2016**. Cardiovascular drugs and therapy / sponsored by the International Society of Cardiovascular Pharmacotherapy 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32621045
ABSTRACT

PURPOSE: The Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results (LEADER) trial showed the cardiovascular disease (CVD) benefits of liraglutide therapy among patients with type 2 diabetes mellitus (T2DM). We applied this trial to US adults with T2DM in terms of eligibility and preventable CVD events. METHODS: We included US adults with T2DM from the National Health and Nutrition Examination Survey (NHANES) 2007-2016. Eligibility criteria from LEADER primary and secondary prevention cohorts were applied to determine potentially eligible US adults. We estimated the number of primary composite and secondary CVD endpoints that would occur based on LEADER treated and placebo published event rates, with the difference indicating the number of preventable events. RESULTS: Among 4672 (projected to 27.3 million [M]) adults we identified with T2DM, we estimated 800 (4.2 million) (15.4%) to fit LEADER eligibility criteria, including 205 (0.9 M) primary prevention 595 (3.3 M) secondary prevention subjects. Compared to LEADER trial participants, our sample had higher proportions of women and minorities, prior angina, chronic kidney disease, and lipid-lowering medication use. We estimated 21,209 primary composite CVD events, 29,691 extended CVD composite outcomes, 16,967 all-cause deaths, 16,967 cardiovascular deaths, 12,725 myocardial infarctions, and 12,725 microvascular events would be prevented annually if our eligible T2DM subjects were on liraglutide. CONCLUSION: Liraglutide may prevent many fatal and non-fatal CVD events if provided to US adults meeting LEADER eligibility criteria. More efforts are needed to educate the healthcare providers on the CVD benefits from newer diabetes therapies, including liraglutide.

[9] *Budoff MJ, Muhlestein JB, Bhatt DL et al.* **Effect of Icosapent Ethyl on Progression of Coronary Atherosclerosis in Patients with Elevated Triglycerides on Statin Therapy: A prospective, placebo-controlled randomized trial (EVAPORATE): Interim Results**. Cardiovascular research 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32609331
ABSTRACT
AIMS: Though statin therapy is known to slow coronary atherosclerosis progression and reduce cardiovascular(CV) events, significant CV risk still remains. In the REDUCE-IT study, icosapent ethyl (IPE) added to statin therapy reduced initial CV events by 25% and total CV events by 30%, but its effects on coronary atherosclerosis progression have not yet been fully investigated. Therefore, this study is to determine whether IPE 4g/d will result in a greater change from baseline in plaque volume measured by serial multidetector computed tomography (MDCT) than placebo in statin-treated patients. METHODS AND RESULTS: EVAPORATE is a randomized, double-blind, placebo-controlled trial. Patients had to have coronary atherosclerosis by coronary computed tomographic angiography CCTA (≥1 angiographic stenoses with ≥20% narrowing), on stable statin therapy with low-density lipoprotein cholesterol levels 40 to 115 mg/dl, and persistently high triglyceride levels (135-499 mg/dL). Patients underwent an interim scan at 9 months and were followed for an additional 9 months with CCTA at 0, 9 and 18 months. Here we present the protocol-specified interim efficacy results.A total of 80 patients were enrolled, with 67 completing the 9-month visit and having interpretable CCTA at baseline and at 9-months (age=57±6 years, male=36, 63%). At the 9-month interim analysis, there was no significant change in low attenuation plaque (LAP) between active and placebo groups (74% vs 94%, p = 0.469). However, there was slowing of total non-calcified plaque (sum of LAP, fibrofatty, and fibrous plaque)(35% v. 43%,p=0.010), total plaque (non-calcified + calcified plaque)(15% v. 26%,p=0.0004), fibrous

plaque (17% v. 40%,p=0.011) and calcified plaque (-1% v. 9%,p=0.001), after adjustment by baseline plaque, age, sex, diabetes, baseline triglyceride levels, and statin use. CONCLUSIONS: EVAPORATE is the first study using CCTA to evaluate the effects of IPE as an adjunct to statin therapy on atherosclerotic plaque characteristics in a high-risk CV population with persistently high TG levels. It provides important mechanistic data in regards to the reduction in CV events in the REDUCE-IT clinical trial. TRANSLATIONAL POTENTIAL: Given the robust cardiovascular event reduction seen in clinical trials of Icosapent ethyl, this study demonstrates that one potential mechanism of benefit of this therapy is to slow atherosclerosis progression. This study shows that most coronary plaque types show slowed rates of progression under the influence of statin plus Icosapent ethyl. A translational use of this information would be to potentially use this therapy in addition to statin therapy in cases with presence of significant atherosclerosis.

[10] *Subczynski WK, Pasenkiewicz-Gierula M*. **Hypothetical Pathway for Formation of Cholesterol Microcrystals Initiating the Atherosclerotic Process**. Cell biochemistry and biophysics 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32602057
ABSTRACT
Major factors leading to the development of atherosclerosis are a high cholesterol (Chol) level in the blood and oxidative stress. Both promote the formation of Chol microcrystals in blood vessel walls. Deposition of Chol microcrystals in arterial intima causes inflammation, which initiates and accompanies the atherosclerotic process in all its phases. One of the possible sources of Chol in the blood vessel walls is oxidized low-density lipoproteins-this atherosclerotic plaque formation pathway has already been described in the literature. Here, we hypothesize that initiation of the atherosclerotic process may involve Chol domains in the plasma membranes of arterial cells. Increased Chol content and the presence of polyunsaturated phospholipids in these membranes together with oxidative stress (phospholipid peroxidation) may lead to the formation of pure Chol bilayer domains that, with further peroxidation and increased Chol content, may collapse in the form of Chol seed crystals. Independent of their origin, Chol microcrystals activate inflammasomes, thereby stimulate immune responses, and initiate inflammation that may lead to the development of atherosclerosis. This new, hypothetical pathway has not yet been investigated in depth; however, data from the literature and our own results support its feasibility.

[11] *Boeckmans J, Natale A, Rombaut M et al.* **Human hepatic in vitro models reveal distinct anti-NASH potencies of PPAR agonists**. Cell Biol Toxicol 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32613381
ABSTRACT
Non-alcoholic steatohepatitis (NASH) is a highly prevalent, chronic liver disease characterized by hepatic lipid accumulation, inflammation, and concomitant fibrosis. Up to date, no anti-NASH drugs have been approved. In this study, we reproduced key NASH characteristics in vitro by exposing primary human hepatocytes (PHH), human skin stem cell-derived hepatic cells (hSKP-HPC), HepaRG and HepG2 cell lines, as well as LX-2 cells to multiple factors that play a role in the onset of NASH. The obtained in vitro disease models showed intracellular lipid accumulation, secretion of inflammatory chemokines, induced ATP content, apoptosis, and increased pro-fibrotic gene expression. These cell systems were then used to evaluate the

anti-NASH properties of eight peroxisome proliferator-activated receptor (PPAR) agonists (bezafibrate, elafibranor, fenofibrate, lanifibranor, pemafibrate, pioglitazone, rosiglitazone, and saroglitazar). PPAR agonists differently attenuated lipid accumulation, inflammatory chemokine secretion, and pro-fibrotic gene expression.Based on the obtained readouts, a scoring system was developed to grade the anti-NASH potencies. The in vitro scoring system, based on a battery of the most performant models, namely PHH, hSKP-HPC, and LX-2 cultures, showed that elafibranor, followed by saroglitazar and pioglitazone, induced the strongest anti-NASH effects. These data corroborate available clinical data and show the relevance of these in vitro models for the preclinical investigation of anti-NASH compounds.

[12] *Amarenco P, Hobeanu C, Labreuche J et al.* **Carotid Atherosclerosis Evolution when Targeting a Low-Density Lipoprotein Cholesterol Concentration < 70 mg/dL after an Ischemic Stroke of Atherosclerotic Origin**. Circulation 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32594766

ABSTRACT
Background: The Treat Stroke to Target (TST) trial showed the benefit of targeting a low-density lipoprotein cholesterol (LDL-C) concentration of <70 mg/dL, in term of reducing the risk of major cardiovascular events in 2860 patients with ischemic stroke with atherosclerotic stenosis of cerebral vasculature. The impact on carotid atherosclerosis evolution is not known. Methods: TST-PLUS (Treat Stroke to Target-PLaque Ultrasound Study) included 201 patients assigned to a LDL-C concentration of <70 mg/dL and 212 patients assigned to a target of 100±10 mg/dL. To achieve these goals, investigators used the statin and dosage of their choice and added ezetimibe as needed. After certification of ultra-sonographers, carotid ultrasound examinations were performed using M'ATH(TM) software at baseline, and at 2, 3, and 5 years. All images were up-loaded to the Intelligence in Medical Technology (IMT(TM)) database directly from the carotid ultrasound device. The central core laboratory performed all off-line measurements of the intima-media thickness of both common carotid arteries blinded from the randomization arm. The main outcomes were newly diagnosed atherosclerotic plaque on carotid bifurcation or internal carotid artery origin using the definition of the Mannheim consensus definition, and the between-group comparison of common carotid arteries intima-media thickness (CCA-IMT) change. Results: After a median follow-up of 3.1 years, the achieved LDL-C concentrations were 64 mg/dL (1.64 mmol/L) in the lower-target group and 106 mg/dL (2.72 mmol/L) in the higher-target group. Compared with the higher target-group, patients in the lower target-group had a similar incidence of newly diagnosed carotid plaque: 46/201, (5-year rate, 26.1%] versus 45/212 (5-year rate, 29.7%). The change in CCA-IMT was -2.69 µm (95% CI, -6.55 to 1.18) in the higher-target group and -10.53 µm (95% CI, -14.21 to -6.85) in the lower-target group, resulting in an absolute between-group difference of -7.84 µm [95% CI, -13.18 to -2.51], P=0.004). Conclusions: In patients with ischemic stroke and atherosclerosis, an LDL-C target of <70 mg/dL (1.8 mmol/L) did not reduce the incidence of new carotid plaques but produced significantly greater regression of carotid atherosclerosis than an LDL-C target of 90 to 110 mg/dL. Clinical Trial Registration: URL: https://clinicaltrials.gov Unique Identifier: NCT01252875.

[13] *Gencer B, Giugliano RP*. **Management of LDL-cholesterol after an acute coronary syndrome: Key comparisons of the American and European clinical guidelines to the attention of the healthcare providers**. Clinical cardiology 2020; 43:684-690.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32596859

ABSTRACT

Guidelines for the management of blood cholesterol were updated in the past year in the United States and Europe, reflecting a more intensive approach to lowering low-density lipoprotein cholesterol (LDL-C). The American College of Cardiology/American Heart Association task force on practice guideline released the 2018 guideline on the management of blood cholesterol on behalf of several American societies. Approximately 9 months later, the European Society of Cardiology/European Atherosclerosis Society published their 2019 guideline for the management of dyslipidemias. Both guidelines have similarities for the management of patients with acute coronary syndromes. Both emphasize risk assessment of patients as a main approach to guide therapy; those at higher risk of cardiovascular disease have a greater clinical benefit of LDL-C reduction by at least 50%. Both guidelines reinforce the indication to lower LDL-C as an important modifiable risk factor and consider the addition of nonstatin agents, such as ezetimibe and proprotein convertase subtilisin kexin 9 (PCSK9) inhibitors, in addition to lifestyle counseling and high-intensity statin for further reduction of LDL-C levels. However, the guidelines have differences in the concepts of treatment thresholds (≥70 mg/dL in the United States) vs treatment goals (< 55 mg/dL in Europe), in the definition of very high-risk category and in the classes for recommendation for the use of PCSK9 inhibitors.

[14] *Barrios V, Escobar C, Arrarte V et al.* **First national registry on the effectiveness and safety of evolocumab in clinical practice in patients attended in cardiology in Spain. The RETOSS-CARDIO study**. Clinica e investigacion en arteriosclerosis : publicacion oficial de la Sociedad Espanola de Arteriosclerosis 2020.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32605806

ABSTRACT

OBJECTIVE: To present the first registry used to analyse the clinical profile of patients treated with evolocumab in Spain, including the effectiveness on the lipid profile and safety in the «real world» setting. METHODS: Multicentre, retrospective, and observational study of patients starting treatment with evolocumab from February 2016 to May 2017 in clinical practice in Spanish cardiology units. RESULTS: A total of 186 patients (mean age 60.3 ± 9.8 years were included, 35.5% with familial hypercholesterolaemia, and 94.1% with a previous cardiovascular event) from 31 cardiology units. Baseline lipid profile: Total cholesterol 219.4 ± 52.2 mg/dL, LDL-cholesterol 144.0 ± 49.0mg/dL, HDL-cholesterol 47.7 ± 13.0mg/dL, and triglycerides 151.0 ± 76.2mg/dL. At the time of initiating evolocumab, 53.8% of patients were taking statins (50% had partial or total intolerance to statins), and 51.1% ezetimibe. In all cases, the dose of evolocumab used was 140 mg, mainly every 2 weeks (97.3%). Evolocumab compliance was high (92.3%). Treatment with evolocumab was interrupted in 6 patients (3.2%), with only 1 (0.5%) due to a probable side effect. Evolocumab significantly reduced total cholesterol (30.9% at week 2, and 39.3% at week 12; P<.001), LDL cholesterol (44.4% and 57.6%, respectively; P<.001), and triglycerides (14.8% and 5.2%, respectively; P<001), with no significant changes in HDL-cholesterol (6.7% and 2.0%; P=.14). CONCLUSIONS: In clinical practice, evolocumab is associated with reductions in LDL cholesterol, with nearly 60% after 12 weeks of treatment, and with low rates of interruptions due to side effects and high medication compliance. These results are consistent with those reported in randomised clinical trials.

[15] *Yang C, Zhang J, Liu C, Xing Y*. **Comparison of the risk factors of hemorrhagic transformation between large artery atherosclerosis stroke and cardioembolism after intravenous thrombolysis**. Clinical neurology and neurosurgery 2020; 196:106032.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32615407

ABSTRACT

OBJECTIVE: Hemorrhagic transformation (HT) is a common complication of ischemic stroke after intravenous thrombolytic therapy (IVT), especially in cardioembolism (CE) and large artery atherosclerosis stroke (LAA) patients. Whether there are different risk factors for HT in LAA and CE patients remains unclear. The aim of this study was to explore the differences in risk factors for HT in patients with LAA and CE after IVT. PATIENTS AND METHODS: A retrospective analysis was conducted on LAA and CE patients who were treated with intravenous tissue plasminogen activator at our hospital from 2015 to 2019. Demographic and clinical information was collected, and HT was evaluated within 72 h after stroke onset. Lipids levels, albumin, uric acid (UA), platelet volume indices, as well as potential predictors of HT were analyzed between patients with and without HT (non-HT group). RESULTS: A total of 247 patients (168 LAA and 79 CE) were included in the study, out of which 62 (25.1 %) had HT. HT was more prevalent in the CE subgroup (30.3 %) than in the LAA subgroup (22.6 %). Compared with non-HT, patients with HT showed a higher rate of the previous stroke, baseline NIHSS scores, and mean platelet volume (MPV), lower levels of platelet count (PC), triglycerides, total cholesterol, low-density lipoprotein cholesterol (LDL-C), albumin, and UA ($P < 0.05$). Multivariate logistic regression analysis showed that lower LDL (OR = 0.547, 95 % CI 0.321-0.932, P = 0.027), and higher blood glucose (OR = 1.137, 95 % CI 1.015-1.247, P = 0.026) were independent risk factors for HT in LAA patients, while lower albumin (OR = 0.989, 95 % CI 0.977-1.000, P = 0.048), and lower PC(OR = 0.868, 95 % CI 0.754-0.989, P = 0.047) were independent risk factors for HT in CE patients. CONCLUSION: Patients with different etiologies may have different risk factors of HT following IVT. Lower LDL-C and higher blood glucose are independent risk factors of LAA, while lower albumin and PC are independent risk factors of CE.

[16] *Zhubi-Bakija F, Bajraktari G, Bytyçi I et al.* **The impact of type of dietary protein, animal versus vegetable, in modifying cardiometabolic risk factors: A position paper from the International Lipid Expert Panel (ILEP)**. Clinical nutrition (Edinburgh, Scotland) 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32620446

ABSTRACT

Proteins play a crucial role in metabolism, in maintaining fluid and acid-base balance and antibody synthesis. Dietary proteins are important nutrients and are classified into: 1) animal proteins (meat, fish, poultry, eggs and dairy), and, 2) plant proteins (legumes, nuts and soy). Dietary modification is one of the most important lifestyle changes that has been shown to significantly decrease the risk of cardiovascular (CV) disease (CVD) by attenuating related risk factors. The CVD burden is reduced by optimum diet through replacement of unprocessed meat with low saturated fat, animal proteins and plant proteins. In view of the available evidence, it has become acceptable to emphasize the role of optimum nutrition to maintain arterial and CV health. Such healthy diets are thought to increase satiety, facilitate weight loss, and improve CV risk. Different studies have compared the benefits of omnivorous and vegetarian diets. Animal protein related risk has been suggested to be greater with red or processed meat over and above poultry, fish and nuts, which carry a lower risk for CVD. In

contrast, others have shown no association of red meat intake with CVD. The aim of this expert opinion recommendation was to elucidate the different impact of animal vs vegetable protein on modifying cardiometabolic risk factors. Many observational and interventional studies confirmed that increasing protein intake, especially plant-based proteins and certain animal-based proteins (poultry, fish, unprocessed red meat low in saturated fats and low-fat dairy products) have a positive effect in modifying cardiometabolic risk factors. Red meat intake correlates with increased CVD risk, mainly because of its non-protein ingredients (saturated fats). However, the way red meat is cooked and preserved matters. Thus, it is recommended to substitute red meat with poultry or fish in order to lower CVD risk. Specific amino acids have favourable results in modifying major risk factors for CVD, such as hypertension. Apart from meat, other animal-source proteins, like those found in dairy products (especially whey protein) are inversely correlated to hypertension, obesity and insulin resistance.

[17] *Tell S, Nadeau KJ, Eckel RH*. **Lipid management for cardiovascular risk reduction in type 1 diabetes**. Current opinion in endocrinology, diabetes, and obesity 2020; 27:207-214.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32618632
ABSTRACT
PURPOSE OF REVIEW: To review the recent evidence for lipid management in type 1 diabetes (T1D) for cardiovascular risk reduction. RECENT FINDINGS: Individuals with T1D are at increased risk for cardiovascular morbidity and mortality, with atherosclerosis beginning as early as adolescence. Elevated low-density lipoprotein cholesterol (LDL-C), triglycerides, and lipoprotein (a) are associated with increased cardiovascular risk in T1D. Although high-density lipoprotein cholesterol (HDL-C) in T1D is often normal or higher than in nondiabetic controls, HDL in T1D has structural alterations, which make it proatherogenic rather than cardioprotective. Similarly, although LDL-C is not particularly elevated in T1D, LDL still contributes to cardiovascular risk. Studies in individuals with diabetes have primarily included T2D participants, with a much smaller number of T1D participants; such studies have shown that lipid-lowering therapies, such as statins, ezetimibe, and proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors reduce LDL-C levels and cardiovascular events in both those with and without diabetes. Individuals with T1D have increased cholesterol absorption, suggesting that ezetimibe may be particularly effective in T1D. Results of the REDUCE-IT trial show cardiovascular risk reduction from high-dose omega-3 fatty acid (Icosapent Ethyl) therapy in patients with diabetes (primarily type 2 diabetes), independent of triglyceride lowering, but similar data in T1D are currently lacking. SUMMARY: Individuals with T1D are at high risk of cardiovascular disease, necessitating close lipid monitoring and management from adolescence through adulthood.

[18] *Soran H, Cooper JA, Durrington PN et al.* **Non-HDL or LDL cholesterol in heterozygous familial hypercholesterolaemia: findings of the Simon Broome Register**. Current opinion in lipidology 2020; 31:167-175.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32618729
ABSTRACT
PURPOSE OF REVIEW: The role of non-HDL-C in the identification and management of lipid disorders is not clearly defined, although UK guidelines recommend its wider use in assessing the need for lipid-lowering therapy and as a treatment target. RECENT FINDINGS: We

examined the implications of the use of non-HDL-C as opposed to LDL-C in 253 people with hypercholesterolaemia before treatment and 573 after treatment in whom fasting total serum cholesterol, HDL-C and LDL-C had been recorded and the diagnosis of heterozygous familial hypercholesterolemia (heFH) was investigated by genetic testing. The difference and the limits of agreement between non-HDL-C and LDL-C calculated using the Friedewald formula were assessed in those with and without heFH-causing mutations. SUMMARY: There were 147 mutation-positive and 106 mutation-negative pretreatment participants and 395 mutation-positive and 178 mutation-negative patients receiving treatment. The difference between non-HDL-C and LDL-C pretreatment in mutation-positive people (mean LDL-C 7.73 mmol/l) was 0.67 mmol/l (95% CI 0.62-0.73) and posttreatment (mean LDL-C 4.71 mmol/l) was 0.62 mmol/l (95% CI 0.59-0.65) with wide limits of agreement of -0.02 to 1.37 and 0.07-1.18 mmol/l, respectively. Among patients with heterozygous familial hypercholesterolaemia, use of estimated LDL-C derived from non-HDL-C in place of calculated LDL-C may result in diagnostic misclassification and difficulty in assessing the true reduction in LDL-C with treatment, because of the wide inter-individual limits of agreement around the mean difference between non-HDL-C and LDL-C.

[19] *Zhao B, Li GP, Peng JJ et al.* **Pitavastatin Combined with Ezetimibe Treatment was an Effective Approach to Non-IRA Lesion of ST-segment Elevation Myocardial Infarc-tion Patients with Primary Percutaneous Coronary Intervention**. Current pharmaceutical biotechnology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32598255
ABSTRACT
OBJECTIVE: ST-segment elevation myocardial infarction (STEMI) patients with the multivessel disease have distinctive plaque characteristics in non-IRA lesions. Intensive statin therapy was a potential approach to treat STEMI patients with the non-IRA disease. However, there is still poor evidence about the therapeutic effect. In this study, we have evaluated the detailed therapeutic effect of statin plus ezetimibe intensive therapy. METHOD: For STEMI patients with non-IRA disease undergoing primary percutaneous coronary intervention (PCI), 183 control STEMI patients without non-IRA disease undergoing primary PCI, and 200 STEMI patients with non-IRA disease undergoing primary PCI were introduced into this study. 200 STEMI patients with non-IRA disease undergoing primary PCI were divided into Normal group, Intensive group, Normal & Combined group, and Intensive & Combined group. The baseline information for each participant was recorded. Meanwhile, the physiological and biochemical indicators of each member with different treatments were collected after one-year follow-up. RESULT: For STEMI patients with non-IRA disease undergoing primary PCI, no differences could be detected in multiple indexes such as OCT examination results, age, stroke, etc. However, diabetes mellitus, smoking, and coronary Gensini score were different between different groups ($P<0.05$). After one year follow-up, cholesterol, low-density lipoprotein, coronary Gensini score, thin-cap fibroatheroma, length of non-infarcted arterial lesions, non-infarct artery lesion range, myocardial infarction again, and revascularization again were significantly different between different groups ($P<0.05$). CONCLUSION: The results mentioned above suggested that pitavastatin combined with ezetimibe was an effective approach to STEMI patients with non-IRA disease undergoing primary PCI. The results obtained in this study have provided a novel way for the treatment of STEMI patients with non-IRA disease undergoing primary PCI.

[20] *Montero E, López M, Vidal H et al.* **Impact of periodontal therapy on systemic markers of inflammation in patients with metabolic syndrome: a randomized clinical trial**. Diabetes Obes Metab 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32613714
ABSTRACT
AIMS: To determine the impact of periodontal treatment on systemic markers of inflammation in patients with metabolic syndrome (MetS) and periodontitis. MATERIAL AND METHODS: In this parallel-arm, double blind, randomized controlled clinical trial, 63 patients with MetS and severe periodontitis were randomly assigned to receive intensive periodontal treatment (IPT; scaling and root planing plus azithromycin 500 mg, q.d., for three days) or minimal periodontal treatment (MPT; supragingival professional mechanical plaque removal plus a placebo). The primary outcome was the impact of the tested interventions on hs-CRP serum levels at 6 months. As secondary outcomes, differences in the levels of cytokines, markers of prothrombotic states, carbohydrate and lipids metabolism, as well as blood pressure, were measured at 3 and 6 months after therapy. RESULTS: The ITT population consisted on 63 subjects randomly assigned to either MPT (n=31) or IPT (n=32) groups. At baseline, mean hs-CRP was 3.9 mg/L (standard deviation, SD=2.9) and 3.9 mg/L (SD=3.4), respectively, and no significant differences in their cardiometabolic risk profiles were detected between groups. Adjusting for baseline hs-CRP, sex, age, smoking status and body mass index, hs-CRP at 6 months was 1.2 mg/L (95% confidence interval, [CI 0.4; 2.0]; p=0.004) lower in the IPT group than in the MPT group. In the secondary outcomes, significant reductions in IL-1β, TNF-α, HbA1c and blood pressure were observed in the IPT group at 3 months, when compared to the MPT group. CONCLUSION: Effective periodontal treatment significantly reduced hs-CRP after 6 months in patients with MetS and severe periodontitis. Periodontal therapy might be useful to reduce cardiovascular risk in these patients.

[21] *Zhai P, Ding Y, Li Y*. **The impact of COVID-19 on ischemic stroke**. Diagn Pathol 2020; 15:78.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32600350
ABSTRACT
BACKGROUND: The outbreak of a novel coronavirus since December 2019, became an emergency of major international concern. As of June 21, 2020, the SARS-CoV-2 pandemic has caused 8,769,844 confirmed infections with 463,745 fatal cases worldwide. The SARS-CoV-2 outbreak is a major challenge for clinicians. In our clinic, we found a rare case that a COVID-19 patient combined with ischemic stroke. CASE PRESENTATION: A 79-year-old man was admitted to the Hubei Provincial Hospital of Traditional Chinese Medicine due to right limb weakness for 1 day and slight cough for 1 week. At presentation, his oxygen saturation was 94.2% on room air and body temperature was 37.3 °C (99.0 °F) with some moist rales. Neurological examination showed right limb weakness, and the limb muscle strength was grade 4. The left leg and arms were unaffected. In addition, runs of speech were not fluent enough with tongue deviation. Laboratory studies showed lymphopenia and eosinophilic granulocytopenia. Chest CT revealed bilateral pulmonary parenchymal ground-glass and consolidative pulmonary opacities, with a peripheral lung distribution. Real-time polymerase chain reaction (RT-PCR) from throat swab sample was positive for SARS-CoV-2 nucleic acid.

This patient was treated with antiviral drugs and anti-inflammatory drugs with supportive care until his discharge. Clopidogrel (75 mg) and atorvastatin (20 mg) were administered orally to treat acute ischemic stroke. After 12 days of treatment, he can walk normally and communicate with near fluent language. CONCLUSION: We report an even more unusual case, a patient who was hospitalized for right limb weakness and was later diagnosed with COVID-19. Here, SARS-CoV-2 infection caused hypoxemia and excessive secretion of inflammatory cytokines, which contribute to the occurrence and development of ischemic stroke. Once COVID-19 patients show acute ischemic stroke, neurologists should cooperate with infectious disease doctors to help patients.

[22] *Shikh E, Zozina V, Kondratenko S et al.* **The particulars of certain drugs' effect on the endogenous coenzyme Q10 plasma level in patients with cardiovascular diseases**. Drug metabolism and personalized therapy 2020; 35.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32609647
ABSTRACT
Objectives Coenzyme Q10 (CoQ10) has many vital functions in human body and its endogenous level can be affected either by various diseases or by administrated drugs. This study reveals the effect of atorvastatin, amlodipine and ethoxidol on the endogenous CoQ10 plasma concentration. Methods It was determined the total plasma concentration of endogenous CoQ10 in the plasma of 54 healthy individuals and 62 patients with cardiovascular diseases during treatment with various drugs using high performance liquid chromatography with mass spectrometric detection (HPLC-MS/MS). Results It was found that CoQ10 plasma concentration in patients is statistically significantly lower (on average -49.0 Δ%) than in practically healthy individuals. The total CoQ10 plasma level in patients receiving atorvastatin in the complex therapy is statistically significantly lower (-15.2 Δ%), and in patients taking amlodipine or ethoxidol is statistically significantly higher (+18.2 and +20.2 Δ%, respectively) than in patients of control groups (a group of patients who receive the same drugs, except for the studied one). Conclusions The study showed that in patients with CVDs treated with various drugs the CoQ10 plasma level is statistically significantly lower than in practically healthy individuals. So, to avoid the adverse reactions connected with low CoQ10 plasma levels, it is recommended to adjust the therapy to maintain its constant level.

[23] *Ferro Y, Mazza E, Salvati M et al.* **Effects of a Portfolio-Mediterranean Diet and a Mediterranean Diet with or without a Sterol-Enriched Yogurt in Individuals with Hypercholesterolemia**. Endocrinol Metab (Seoul) 2020; 35:298-307.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32615714
ABSTRACT
BACKGROUND: A growing number of functional foods have been proposed to reduce cholesterol levels and the Portfolio Diet, which includes a combination of plant sterols, fibres, nuts, and soy protein, reduces low density lipoprotein cholesterol (LDL-C) from 20% to 30% in individuals with hyperlipidaemia. In this pilot study, the aim was to investigate whether a Mediterranean Diet incorporating a new and simple combination of cholesterol-lowering foods, excluding soy and nuts (namely the Portfolio-Mediterranean Diet), would reduce LDL-C levels, in the short-term, better than a Mediterranean Diet plus a sterol-enriched yogurt or a Mediterranean Diet alone. METHODS: We retrospectively evaluated 24 individuals on a Portfolio-Mediterranean Diet and 48 matched individuals on a Mediterranean Diet with or

without a sterol-enriched yogurt (24 each groups) as controls. RESULTS: At follow-up (after 48±12 days), we observed an LDL reduction of 21±4, 23±4, and 44±4 mg/dL in the Mediterranean Diet alone, Mediterranean Diet plus yogurt and Portfolio-Mediterranean Diet respectively (P<0.001). CONCLUSION: A Portfolio-Mediterranean Diet, incorporating a new combination of functional foods such as oats or barley, plant sterols, chitosan, and green tea but not soy and nuts, may reduce LDL of 25% in the short term in individuals with hypercholesterolemia.

[24] *Han E, Cho NH, Moon SS, Cho H*. **Comparison of Serum PCSK9 Levels in Subjects with Normoglycemia, Impaired Fasting Glucose, and Impaired Glucose Tolerance**. Endocrinol Metab (Seoul) 2020; 35:480-483.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32615732
ABSTRACT
We investigated proprotein convertase subtilisin/kexin type 9 (PCSK9) concentrations in individuals with normoglycemia, impaired fasting glucose (IFG), and impaired glucose tolerance (IGT). This was a pilot, cross-sectional study including 92 individuals who had not been diagnosed with or treated for diabetes. We measured PCSK9 levels in three groups of subjects; namely, normoglycemia (n=57), IFG (n=21), and IGT (n=14). Individuals with IFG and IGT showed higher PCSK9 concentrations than those in the normoglycemic group, with the highest serum PCSK9 concentrations found in individuals with IGT (55.25±15.29 ng/mL for normoglycemia, 63.47±17.78 ng/mL for IFG, 72.22±15.46 ng/mL for IGT, analysis of variance P=0.001). There were no significant differences in high- or low-density lipoprotein cholesterol among groups. Serum PCSK9 levels are increased in patients with prediabetes compared to subjects with normoglycemia.

[25] *Lee SH, Kim MK, Rhee EJ*. **Effects of Cardiovascular Risk Factor Variability on Health Outcomes**. Endocrinol Metab (Seoul) 2020; 35:217-226.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32615706
ABSTRACT
Innumerable studies have suggested "the lower, the better" for cardiovascular risk factors, such as body weight, lipid profile, blood pressure, and blood glucose, in terms of health outcomes. However, excessively low levels of these parameters cause health problems, as seen in cachexia, hypoglycemia, and hypotension. Body weight fluctuation is related to mortality, diabetes, obesity, cardiovascular disease, and cancer, although contradictory findings have been reported. High lipid variability is associated with increased mortality and elevated risks of cardiovascular disease, diabetes, end-stage renal disease, and dementia. High blood pressure variability is associated with increased mortality, myocardial infarction, hospitalization, and dementia, which may be caused by hypotension. Furthermore, high glucose variability, which can be measured by continuous glucose monitoring systems or self-monitoring of blood glucose levels, is associated with increased mortality, microvascular and macrovascular complications of diabetes, and hypoglycemic events, leading to hospitalization. Variability in metabolic parameters could be affected by medications, such as statins, antihypertensives, and hypoglycemic agents, and changes in lifestyle patterns. However, other mechanisms modify the relationships between biological variability and various health outcomes. In this study, we review recent evidence regarding the role of variability in metabolic parameters and discuss the clinical implications of these findings.

[26] *Kristiansen O, Vethe NT, Peersen K et al.* **Effect of atorvastatin on muscle symptoms in coronary heart disease patients with self-perceived statin muscle side-effects: a randomized, double blinded crossover trial**. European heart journal. Cardiovascular pharmacotherapy 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32609361
ABSTRACT
AIMS: To estimate the effect of atorvastatin on muscle symptom intensity in coronary heart disease (CHD) patients with self-perceived statin-associated muscle symptoms (SAMS) and to determine the relationship to blood levels of atorvastatin and/or metabolites. METHODS AND RESULTS: A randomized multi-center trial consecutively identified 982 patients with previous or ongoing atorvastatin treatment after a CHD event. Of these, 97 (9.9%) reported SAMS and 77 were randomized to 7-weeks double-blinded treatment with atorvastatin 40 mg/day and placebo in a crossover design. The primary outcome was the individual mean difference in muscle symptom intensity between the treatment periods, measured by visual-analogue scale (VAS) scores. Atorvastatin did not affect the intensity of muscle symptoms among 71 patients who completed the trial. Mean VAS difference [statin-placebo] was 0.31 (95% CI -0.24-0.86). The proportion with more muscle symptoms during placebo than atorvastatin was 17% (n = 12), 55% (n = 39) had the same muscle symptom intensity during both treatment periods whereas 28% (n = 20) had more symptoms during atorvastatin than placebo (confirmed SAMS). There were no differences in clinical or pharmacogenetic characteristics between these groups. The levels of atorvastatin and/or metabolites did not correlate to muscle symptom intensity among patients with confirmed SAMS (Spearmans rho ≤0.40, for all variables). CONCLUSION: Re-challenge with high-intensity atorvastatin did not affect the intensity of muscle symptoms in CHD patients with self-perceived SAMS during previous atorvastatin therapy. There was no relationship between muscle symptoms and the systemic exposure to atorvastatin and/or its metabolites. The findings encourage an informed discussion to elucidate other causes of muscle complaints and continued statin use.

[27] *Goldberg H, Mohsin FK, Saskin R et al.* **The Suggested Unique Association Between the Various Statin Subgroups and Prostate Cancer**. Eur Urol Focus 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32620539
ABSTRACT
BACKGROUND: The chemopreventive effect of various medications in prostate cancer (PCa) has gained interest. Specifically, the potential impact of statins on PCa incidence has been studied, but solely as a "drug family" overlooking the distinctive pharmacological properties of its two main subgroups: hydrophilic and hydrophobic statins. OBJECTIVE: To assess the impact of statin subgroups on PCa-specific mortality (PCSM), PCa diagnosis, and undergoing another prostate biopsy. DESIGN, SETTING, AND PARTICIPANTS: This is a population-based cohort study in Ontario identifying all men aged ≥66 yr with a history of a single negative prostate biopsy (representing healthy men at risk for PCa) between 1994 and 2016, who were not on any of the analyzed medications prior to the study, with a median follow-up of 9.42 yr (interquartile range 8.03 yr). OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: Using multivariable cause-specific hazard models with time-dependent covariates, the association of hydrophobic and hydrophilic statins with all study outcomes was analyzed. Other putative chemopreventive medications (including alpha-blockers, 5-alpha-reductase

inhibitors, and proton-pump inhibitors), age, rurality, comorbidities, and study inclusion year were included in the models. RESULTS AND LIMITATIONS: Overall, 21 512 men were identified. Statins were taken by 11 401 patients (50.3%), 5184 men (24.1%) were diagnosed with PCa, and 805 (3.7%) died from it. Overall, 7556 patients (35.1%) underwent another biopsy. Any use of hydrophilic statins was associated with a 32.4% (95% confidence interval [CI] 12.9-47.5%), a 20% (95% CI 10-28%), and an 18% (95% CI 6.1-27.3%) decreased risk of PCSM, undergoing another prostate biopsy, and being diagnosed with PCa, respectively. Hydrophobic statins were associated with 17% (95% CI 2-31%) decreased PCSM. The study is limited by its retrospective nature, selection bias, and accompanying health-administrative database inaccuracies. CONCLUSIONS: Use of any statin may be associated with a lower hazard of PCSM, with hydrophilic statins showing a greater association with decreased PCa diagnosis rates. Preferentially prescribing one statin subgroup over another in men needs further exploration. PATIENT SUMMARY: Use of any statin may be associated with a lower probability of dying from prostate cancer. Hydrophilic statins (rosuvastatin and pravastatin) may also be more positively associated with a lower risk of undergoing an additional prostate biopsy and being diagnosed with prostate cancer in men aged ≥66 yr.

[28] *van Bruggen FH, Nijhuis GBJ, Zuidema SU, Luijendijk H*. **Serious adverse events and deaths in PCSK9 inhibitor trials reported on ClinicalTrials.gov: a systematic review**. Expert Rev Clin Pharmacol 2020:1-10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32597252
ABSTRACT
BACKGROUND: Previous reviews of PCSK9 inhibitor trials are limited by a focus on composite cardiovascular outcomes. ClinicalTrials.gov provides trial results for individual clinical outcomes. Aim of this systematic review was to assess the effect of PCSK9 inhibitors on the risk of myocardial infarction, stroke/TIA, heart failure, diabetes mellitus, neurocognitive events, all-cause serious adverse events (SAE), and all-cause deaths as registered on ClinicalTrials.gov. METHODS: PubMed, regulatory reports, ClinicalTrials.gov, and company websites were used to search studies. Randomized trials comparing PCSK9 inhibitor with placebo in participants with hypercholesterolemia were eligible. Study characteristics, risk of bias, and numbers of participants with the outcomes of interest were collected. RESULTS: We identified 33 lipid-lowering and 4 clinical outcomes trials with results on ClinicalTrials.gov (n = 16,958 and n = 73,836, respectively). Risk of bias was generally high. PCSK9 inhibitors did not affect the risk of any of the investigated outcomes in either type of trial. However, in clinical outcomes studies, alirocumab decreased the risk of all-cause SAE (OR 0.92; 95% CI 0.86-0.98), and evolocumab probably increased the risk of mortality (OR 1.12; 95% CI 1.00-1.25). CONCLUSIONS: Our meta-analysis of clinical events registered on ClinicalTrials.gov did not show that PCSK9 inhibitors improve cardiovascular health. Evolocumab increased the risk of all-cause mortality.

[29] *O'Connell EM, Lohoff FW*. **Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) in the Brain and Relevance for Neuropsychiatric Disorders**. Frontiers in neuroscience 2020; 14:609.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32595449
ABSTRACT

Proprotein convertase subtilisin/kexin type 9 (PCSK9) has long been studied in the liver due to its regulation of plasma low-density lipoprotein cholesterol (LDL-C) and its causal role in familial hypercholesterolemia. Although PCSK9 was first discovered in cerebellar neurons undergoing apoptosis, its function in the central nervous system (CNS) is less clear. PCSK9 has been shown to be involved in neuronal differentiation, LDL receptor family metabolism, apoptosis, and inflammation in the brain, but in vitro and in vivo studies offer contradictory findings. PCSK9 expression in the adult brain is low but is highly upregulated during disease states. Cerebral spinal fluid (CSF) PCSK9 concentrations are correlated with neural tube defects and neurodegenerative diseases in human patients. Epigenetic studies reveal that chronic alcohol use may modulate methylation of the PCSK9 gene and genetic studies show that patients with gain-of-function PCSK9 variants have higher LDL-C and an increased risk of ischemic stroke. Early safety studies of the PCSK9 inhibitors evolocumab and alirocumab, used to treat hypercholesterolemia, hinted that PCSK9 inhibition may negatively impact cognition but more recent, longer-term clinical trials found no adverse neurocognitive events. The purpose of this review is to elucidate the role of PCSK9 in the brain, particularly its role in disease pathogenesis.

[30] *Imazio M, Andreis A, Brucato A et al.* **Colchicine for acute and chronic coronary syndromes**. Heart 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32611559
ABSTRACT
Colchicine is an ancient drug, traditionally used for the treatment and prevention of gouty attacks; it has become standard of treatment for pericarditis with a potential role in the treatment of coronary artery disease. Atherosclerotic plaque formation, progression, destabilisation and rupture are influenced by active proinflammatory cytokines interleukin (IL)-1β and IL-18 that are generated in the active forms by inflammasomes, which are cytosolic multiprotein oligomers of the innate immune system responsible for the activation of inflammatory responses. Colchicine has a unique anti-inflammatory mechanism: it is not only able to concentrate in leucocytes, especially neutrophils, and block tubulin polymerisation, affecting the microtubules assembly, but also inhibits (NOD)-like receptor protein 3 (NLRP3) inflammasome. On this basis, colchicine interferes with several functions of leucocytes and the assembly and activation of the inflammasome as well, reducing the production of interleukin 1β and interleukin 18. Long-term use of colchicine has been associated with a reduced rate of cardiovascular events both in chronic and acute coronary syndromes, with an overall good safety profile. This review will focus on the influence of colchicine on the pathophysiology of coronary artery disease, reviewing essential pharmacology and discussing the most important and recent clinical studies. On the basis of current literature, colchicine is emerging as a possible new valuable, safe and cheap agent for the treatment of acute and chronic coronary syndromes.

[31] *Andrade C*. **Nonfasting Lipid Profile May Suffice to Manage Dyslipidemia**. Indian J Psychol Med 2020; 42:316-317.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32612341
ABSTRACT
Patients with major mental illness and especially those who receive antipsychotic drugs are at increased risk of metabolic syndrome. Dyslipidemia is part of the metabolic syndrome.

Dyslipidemia is associated with an increased risk of cardiovascular, cerebrovascular, and other diseases. A fasting lipid profile is traditionally ordered to determine the need for and to monitor lipid-lowering treatment. However, a recent study showed that fasting and nonfasting lipid levels, obtained from the same patients, almost identically predicted hard 3-year cardiovascular event risks; the risks with fasting and nonfasting levels were closely similar in various secondary analyses, as well. This supports the stance of major medical associations in the field to accept nonfasting lipid levels to guide the treatment of dyslipidemia in the primary and secondary prevention of cardiovascular and cerebrovascular disease events.

[32] *Vats P, Das B, Khanra S*. **Serum Lipids among Drug Naïve or Drug-Free Patients with Obsessive Compulsive Disorder and their Association with Impulsivity: A Comparative Study**. Indian J Psychol Med 2020; 42:281-289.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32612334

ABSTRACT

BACKGROUND: The derangement of serum lipids is well documented in psychiatric disorders like schizophrenia, mania, and depression but not in obsessive compulsive disorder (OCD), where it has been inadequately examined. Also, serum lipid abnormalities are increasingly found in "impulsivity," an important sub-construct of OCD. Our study aimed to examine serum lipid profile among patients with OCD and its association with clinical profile and impulsivity among them. METHODS: Forty drug naïve or drug-free (four weeks for oral and eight weeks for any depot psychotropics) patients with OCD according to International Classification of Disease -10(th) version (ICD-10): Diagnostic Criteria for Research (DCR) by the World Health Organization (WHO), from outpatient and inpatient departments of a tertiary care psychiatric hospital were recruited. Measures like Yale-Brown Obsessive Compulsive Scale (Y-BOCS), Hamliton Rating Scale for Depression (HAM-D), Barratt's Impulsivity Scale (BIS-11), and Hamilton Rating Scale for Anxiety (HAM-A) were administered. Forty age and sex-matched healthy controls (HC) were recruited after screening with General Health Questionnaire 12 (GHQ-12). Serum lipids were assessed in both the groups. RESULTS: Serum high density lipoproteins (HDL) ($P < 0.001$; partial $\eta(2) = 0.176$) and apolipoprotein B ($P < 0.001$; partial $\eta(2) = 0.531$) were significantly higher in OCD group than age- and sex-matched HC. A trend toward lower serum HDL ($P = 0.06$; partial $\eta(2) = 0.060$) was observed among patients of OCD with high impulsivity. Serum HDL was negatively correlated with BIS attention ($r(s) = -0.32$; $p = 0.03$), BIS motor ($r(s) = 0.40$; $P = 0.01$), BIS non-planning ($r(s) = - 0.36$; $P = 0.02$), and BIS total ($r(s) = - 0.36$; $P = 0.01$) scores. Serum triglycerides (TG) ($r(s) = 0.34$; $P = 0.03$) and apolipoprotein B ($r(s) = -0.32$; $P = 0.04$) were negatively correlated with Y-BOCS compulsion score. Serum TG ($r(s) = -0.45$, $P < 0.01$) and serum very low density lipoprotein (VLDL) was negatively ($r(s) = -0.39$; $P = 0.01$) correlated with Y-BOCS total scores. Serum VLDL was positively ($r(s) = 0.34$; $P = 0.03$) correlated with BIS motor scores. CONCLUSIONS: Serum lipid fractions are deranged among patients with OCD. Different lipid fractions have different associations with clinical profiles of OCD. Impulsivity among patients with OCD may have a specific association with serum lipids. A small sample size, use of self-report measure without adaptation for impulsivity, a lack of metabolic profile assessment among participants, and a lack of assessment of impulsivity among HC were the limitations of our tudy.

[33] *Shiga Y, Idemoto Y, Tashiro K et al.* **Regression and Stabilization of Coronary Vulnerable Plaque by Evolocumab as Assessed by Multidetector Row Computed Tomography**. Intern Med 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32611955
ABSTRACT
A 65-year-old man was followed for his coronary conditions using 320-multidetector row computed tomography (MDCT) for 30 months. He had soft plaque in the right coronary artery (RCA) [mean density of plaque was 22 hounsfield units (HU). His initial serum low-density lipoprotein cholesterol (LDL-C) was 72 mg/dL. After 30 months, his serum LDL-C was 26 mg/dL under 5.0 mg/day rosuvastatin and evolocumab 140 mg/2 weeks. MDCT showed a regression of the plaque in the RCA and the plaque density was 114 HU (intermediate plaque). In conclusion, intensive lipid-lowering therapy with evolocumab induced the regression and stabilization of coronary vulnerable plaque.

[34] *Laird E, Rhodes J, Kenny RA*. **Vitamin D and Inflammation: Potential Implications for Severity of Covid-19**. Ir Med J 2020; 113:81.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32603576
ABSTRACT
Background Recent research has indicated that vitamin D may have immune supporting properties through modulation of both the adaptive and innate immune system through cytokines and regulation of cell signalling pathways. We hypothesize that vitamin D status may influence the severity of responses to Covid-19 and that the prevalence of vitamin D deficiency in Europe will be closely aligned to Covid-19 mortality. Methods We conducted a literature search on PubMed (no language restriction) of vitamin D status (for older adults) in countries/areas of Europe affected by Covid-19 infection. Countries were selected by severity of infection (high and low) and were limited to national surveys or where not available, to geographic areas within the country affected by infection. Covid-19 infection and mortality data was gathered from the World Health Organisation. Results Counter-intuitively, lower latitude and typically 'sunny' countries such as Spain and Italy (particularly Northern Italy), had low mean concentrations of 25(OH)D and high rates of vitamin D deficiency. These countries have also been experiencing the highest infection and death rates in Europe. The northern latitude countries (Norway, Finland, Sweden) which receive less UVB sunlight than Southern Europe, actually had much higher mean 25(OH)D concentrations, low levels of deficiency and for Norway and Finland, lower infection and death rates. The correlation between 25(OH)D concentration and mortality rate reached conventional significance (P=0.046) by Spearman's Rank Correlation. Conclusions Optimising vitamin D status to recommendations by national and international public health agencies will certainly have benefits for bone health and potential benefits for Covid-19. There is a strong plausible biological hypothesis and evolving epidemiological data supporting a role for vitamin D in Covid-19.

[35] *Johri AM, Nambi V, Naqvi TZ et al.* **Recommendations for the Assessment of Carotid Arterial Plaque by Ultrasound for the Characterization of Atherosclerosis and Evaluation of Cardiovascular Risk: From the American Society of Echocardiography**. Journal of the American Society of Echocardiography : official publication of the American Society of Echocardiography 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32600741

ABSTRACT
Atherosclerotic plaque detection by carotid ultrasound provides cardiovascular disease risk stratification. The advantages and disadvantages of two-dimensional (2D) and three-dimensional (3D) ultrasound methods for carotid arterial plaque quantification are reviewed. Advanced and emerging methods of carotid arterial plaque activity and composition analysis by ultrasound are considered. Recommendations for the standardization of focused 2D and 3D carotid arterial plaque ultrasound image acquisition and measurement for the purpose of cardiovascular disease stratification are formulated. Potential clinical application towards cardiovascular risk stratification of recommended focused carotid arterial plaque quantification approaches are summarized.

[36] *Collinson P, Kiely P*. **Unexpected Troponin Elevation in a Patient Treated with Atorvastatin**. J Appl Lab Med 2020; 5:798-801.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32603445
ABSTRACT

[37] *Qu F, Chen R, Peng Y et al.* **Assessment of the Predictive Role of Serum Lipid Profiles in Breast Cancer Patients Receiving Neoadjuvant Chemotherapy**. J Breast Cancer 2020; 23:246-258.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32595987
ABSTRACT
PURPOSE: Effective predictors of the response to neoadjuvant chemotherapy (NAC) are still insufficient. This study aimed to investigate the predictive value of serum lipid profiles for the response to NAC in breast cancer patients. METHODS: A total of 533 breast cancer patients who had received NAC were retrospectively studied. The pretreatment of serum lipids, including total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and lipoprotein-α, and clinicopathological characteristics were collected to assess their predictive roles. RESULTS: Breast cancer patients had significantly lower TC, TG, HDL-C, and LDL-C levels than normal individuals. Among these indicators, TG and LDL-C levels and HDL-C level increased and decreased significantly after NAC, respectively. In estrogen receptor (ER)-positive patients, increased LDL-C level was associated with better outcomes. Moreover, the receiver operating characteristic curve analyses suggested that TG and HDL-C levels at diagnosis can be used as predictors of the response to NAC only in the ER-positive subgroup. According to univariate analyses, patients with low TG level (< 1.155 mmol/L) or high HDL-C level (≥ 1.305 mmol/L) in the ER-positive subgroup had more favorable clinical responses than the other patients in the subgroup. Furthermore, according to multivariate analyses, a high HDL-C level (≥ 1.305 mmol/L, p = 0.007) was an independent predictor of NAC efficacy. CONCLUSION: High HDL-C level (≥ 1.305 mmol/L) before NAC and increased LDL-C level after NAC were associated with the better treatment response in ER-positive breast cancer patients. These results are potentially considered beneficial in establishing treatment decisions.

[38] *Farshidi H, Sobhani AR, Eslami M et al.* **Magnesium Sulfate Administration in Moderate Coronary Artery Disease Patients Improves Atherosclerotic Risk Factors: A Double Blind Clinical Trial Study**. Journal of cardiovascular pharmacology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32618829

ABSTRACT
Magnesium (Mg) deficiency is known to promote vascular and cardiac dysfunctions such as atherosclerosis. This study investigated the effect of oral MgSO4 therapy to improve lipid profile and serum oxidized LDL (oxLDL) level and its receptor (LOX1) in moderate coronary atherosclerotic patients. In this randomized double blind placebo-controlled clinical trial study, sixty-four patients with moderate coronary artery disease were selected according to angiography findings. Participants were divided into two groups including Mg-treated (n=32) and placebo(n=32) The patients received either placebo or MgSO4 supplement capsule containing 300 mg MgSO4 for 6 months on a daily basis. Lipid profile, HbA1c, 2h postprandial (2hpp) blood glucose, fasting blood sugar (FBS), serum SGOT, SGPT, ox-LDL and lectin-like ox-LDL receptor 1(LOX1) concentrations were measured at baseline and every three months. HbA1c, serum LOX1 and oxLDL concentrations were significantly lower in Mg-treated than placebo group three months after MgSO4 administration. 2hpp, serum LDL-C, SGPT, SGOT levels and HbA1c levels significantly improved in Mg-treated group compared to placebo received group. Overall, the results of this study showed that magnesium treatment improved some of the major risk factors of atherosclerosis. According to the results of liver function tests (SGOT and SGPT), magnesium therapy seems to be safe in patients with moderate atherosclerotic plaque. Therefore, it is suggested that magnesium to be used along with other atherosclerosis control drugs.

[39] *Teoh N, Farrell G*. **Statins as early therapy to mitigate COVID-19 (SARS-CoV-2)-associated ARDS and cytokine storm syndrome - time is of the essence**. J Clin Transl Res 2020; 5:227-229.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32617428
ABSTRACT

[40] *Fedak A, Ciuk K, Urbanik A*. **Ultrasonography of vulnerable atherosclerotic plaque in the carotid arteries: B-mode imaging**. Journal of ultrasonography 2020; 20:e135-e145.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32609972
ABSTRACT
The most common type of stroke, i.e. ischemic stroke, is a great challenge for contemporary medicine as it poses both diagnostic and therapeutic difficulties. Atherosclerosis, which is rapidly beginning to affect more and more social groups, is the main cause of cerebrovascular accidents. Atherosclerosis is currently defined as a generalized, dynamic and heterogeneous inflammatory and immune process affecting arterial walls. Atherosclerotic plaque is the emanation of this disease. As the paradigm of the diagnosis of atherosclerosis has changed, it has become crucial to properly identify plaque instability within the carotid arteries by evaluating parameters and phenomena that signify a developing cascade of complications, eventually leading to stroke. Irrespective of the ultrasound technique employed, proper morphological evaluation of atherosclerotic plaque, involving observation of its echogenicity, i.e. subjective analysis of its structure, with the classification to Gray-Weale-Nicolaides types as well as assessment of the integrity of its surface, makes it possible to roughly evaluate plaque morphology and thereby its stability. This enables treatment planning and therapy monitoring. This evaluation should be a prelude to further diagnostic work-up, which involves non-invasive examinations that enable unambiguous assessment of plaque stability. These examinations include contrast-enhanced ultrasound to assess progression or recession of

inflammation, which presents as plaque neovascularization, or shear wave elastography to objectively define tissue stiffness, and thereby its mineralization. The most common type of stroke, i.e. ischemic stroke, is a great challenge for contemporary medicine as it poses both diagnostic and therapeutic difficulties. Atherosclerosis, which is rapidly beginning to affect more and more social groups, is the main cause of cerebrovascular accidents. Atherosclerosis is currently defined as a generalized, dynamic and heterogeneous inflammatory and immune process affecting arterial walls. Atherosclerotic plaque is the emanation of this disease. As the paradigm of the diagnosis of atherosclerosis has changed, it has become crucial to properly identify plaque instability within the carotid arteries by evaluating parameters and phenomena that signify a developing cascade of complications, eventually leading to stroke. Irrespective of the ultrasound technique employed, proper morphological evaluation of atherosclerotic plaque, involving observation of its echogenicity, i.e. subjective analysis of its structure, with the classification to Gray-Weale–Nicolaides types as well as assessment of the integrity of its surface, makes it possible to roughly evaluate plaque morphology and thereby its stability. This enables treatment planning and therapy monitoring. This evaluation should be a prelude to further diagnostic work-up, which involves non-invasive examinations that enable unambiguous assessment of plaque stability. These examinations include contrast-enhanced ultrasound to assess progression or recession of inflammation, which presents as plaque neovascularization, or shear wave elastography to objectively define tissue stiffness, and thereby its mineralization.

[41] *Chemello K, Beeské S, Trang Tran TT et al.* **Lipoprotein(a) Cellular Uptake Ex Vivo and Hepatic Capture In Vivo Is Insensitive to PCSK9 Inhibition With Alirocumab**. JACC. Basic to translational science 2020; 5:549-557.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32613143
ABSTRACT
Lipoprotein(a) (Lp[a]) is the most common genetically inherited risk factor for cardiovascular disease. Many aspects of Lp(a) metabolism remain unknown. We assessed the uptake of fluorescent Lp(a) in primary human lymphocytes as well as Lp(a) hepatic capture in a mouse model in which endogenous hepatocytes have been ablated and replaced with human ones. Modulation of LDLR expression with the PCSK9 inhibitor alirocumab did not alter the cellular or the hepatic uptake of Lp(a), demonstrating that the LDL receptor is not a major route for Lp(a) plasma clearance. These results have clinical implications because they underpin why statins are not efficient at reducing Lp(a).

[42] *Banach M, Duell PB, Gotto AM, Jr. et al.* **Association of Bempedoic Acid Administration With Atherogenic Lipid Levels in Phase 3 Randomized Clinical Trials of Patients With Hypercholesterolemia**. JAMA cardiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32609313
ABSTRACT
IMPORTANCE: Additional lipid-lowering therapy options are needed for patients who cannot achieve sufficient decreases in low-density lipoprotein cholesterol (LDL-C) levels using statins alone or for those who are statin intolerant. OBJECTIVE: To conduct a pooled analysis of phase 3 randomized clinical trials of bempedoic acid vs placebo. DESIGN, SETTING, AND PARTICIPANTS: This analysis pooled data from 4 double-blind, placebo-controlled randomized clinical trials conducted from 2016 to 2018. Patients were enrolled in North

America and Europe. Eligibility criteria included hypercholesterolemia while receiving stable lipid-lowering therapy and high cardiovascular risk or hypercholesterolemia and statin intolerance. INTERVENTIONS: Patients were randomized 2:1 to bempedoic acid, 180 mg (n = 2425), or placebo (n = 1198) once daily for 12 to 52 weeks. MAIN OUTCOMES AND MEASURES: Primary efficacy end point was percentage change from baseline in LDL-C level at week 12 in the intention-to-treat population. Patients were parsed into 2 groups according to enrollment criteria: (1) patients with hypercholesterolemia and atherosclerotic cardiovascular disease (ASCVD) or with heterozygous familial hypercholesterolemia (HeFH) or with both and receiving statins and (2) patients with hypercholesterolemia who were statin intolerant receiving maximally tolerated statins. RESULTS: In this analysis of 3623 patients, the overall mean (SD) patient age was 65.5 (9.2) years (similar in both pools). Among patients with ASCVD or HeFH or both, the mean (SD) baseline LDL-C level was 107.6 (32.7) mg/dL. At week 12, the LDL-C level percentage change from baseline was -16.0% with bempedoic acid vs 1.8% with placebo (difference, -17.8%; 95% CI, -19.5% to -16.0%; P < .001). Patients with statin intolerance had a mean (SD) baseline LDL-C level of 144.4 (38.8) mg/dL. The percentage changes in LDL-C levels at week 12 were -23.0% in the bempedoic acid group and 1.5% in the placebo group (difference, -24.5%; 95% CI, -27.8% to -21.1%; P < .001). The decrease in LDL-C levels with bempedoic acid was sustained during long-term follow-up in both pools (patients with ASCVD or HeFH or both receiving a maximally tolerated statin, difference of -12.7% at week 52; patients with statin intolerance, difference of -22.2% at week 24). Decreases in non-high-density lipoprotein cholesterol, total cholesterol, apolipoprotein B, and high-sensitivity C-reactive protein levels were greater with bempedoic acid vs placebo. Treatment-emergent adverse events associated more frequently with bempedoic acid than with placebo included increased blood uric acid level (2.1% vs 0.5%), gout (1.4% vs 0.4%), decreased glomerular filtration rate (0.7% vs <0.1%), and increased levels of hepatic enzymes (2.8% vs 1.3%). CONCLUSIONS AND RELEVANCE: Bempedoic acid added to maximally tolerated statins, including moderate- or high-intensity statins or no background statin, was associated with decreased LDL-C levels vs placebo in patients with hypercholesterolemia with an acceptable safety profile. As a nonstatin adjunct or statin alternative, bempedoic acid has potential for use in a broad spectrum of patients. TRIAL REGISTRATION: ClinicalTrials.gov Identifiers: NCT02666664, NCT02991118, NCT03001076, and NCT02988115.

[43] *Kopacz A, Werner E, Grochot-Przęczek A et al.* **Simvastatin Attenuates Abdominal Aortic Aneurysm Formation Favoured by Lack of Nrf2 Transcriptional Activity**. Oxidative medicine and cellular longevity 2020; 2020:6340190.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32617140

ABSTRACT

Surgical intervention is currently the only option for an abdominal aortic aneurysm (AAA), preventing its rupture and sudden death of a patient. Therefore, it is crucial to determine the pathogenic mechanisms of this disease for the development of effective pharmacological therapies. Oxidative stress is said to be one of the pivotal factors in the pathogenesis of AAAs. Thus, we aimed to evaluate the significance of nuclear factor erythroid 2-related factor 2 (Nrf2) transcriptional activity in the development of AAA and to verify if simvastatin, administered as pre- and cotreatment, may counteract this structural malformation. Experiments were performed on mice with inhibited transcriptional activity of Nrf2 (tKO) and wild-type (WT) counterparts. We used a model of angiotensin II- (AngII-) induced AAA, combined with a fat-

enriched diet. Mice were administered with AngII or saline for up to 28 days via osmotic minipumps. Simvastatin administration was started 7 days before the osmotic pump placement and then continued until the end of the experiment. We found that Nrf2 inactivation increased the risk of development and rupture of AAA. Importantly, these effects were reversed by simvastatin in tKO mice, but not in WT. The abrupt blood pressure rise induced by AngII was mitigated in simvastatin-treated animals regardless of the genotype. Simvastatin-affected parameters that differed between the healthy structure of the aorta and aneurysmal tissue included immune cell infiltration of the aortic wall, VCAM1 mRNA and protein level, extracellular matrix degradation, TGF-β1 mRNA level, and ERK phosphorylation, but neither oxidative stress nor the level of Angiotensin II Type 1 Receptor (AT1R). Taken together, the inhibition of Nrf2 transcriptional activity facilitates AAA formation in mice, which can be prevented by simvastatin. It suggests that statin treatment of patients with hypercholesterolemia might have not only a beneficial effect in terms of controlling atherosclerosis but also potential AAA prevention.

[44] *Gadiparthi C, Bassi M, Yegneswaran B et al.* **Hyperglycemia, Hypertriglyceridemia, and Acute Pancreatitis in COVID-19 Infection: Clinical Implications**. Pancreas 2020; 49:e62-e63.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32604205
ABSTRACT

[45] *Xie W, Huang H, Xiao S et al.* **Effect of statin use on cardiovascular events and all-cause mortality in immune-mediated inflammatory diseases: A systematic review and meta-analysis involving 148,722 participants**. Pharmacological research : the official journal of the Italian Pharmacological Society 2020; 160:105057.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32619724
ABSTRACT
BACKGROUND: Immune-mediated inflammatory diseases (IMIDs) are associated with an increased risk of premature cardiovascular disease and all-cause mortality. Given lipid-lowering and anti-inflammatory properties, statins theoretically provide greater survival benefits for patients with IMIDs. OBJECTIVE: We aimed to evaluate the impact of statin on all-cause mortality and cardiovascular risk in patients with IMIDs, and examine whether the effect varies between primary prevention and secondary prevention. METHODS: We systematically searched PubMed, EMBASE and Cochrane Library to identify eligible studies evaluating the association between statin use and all-cause mortality or cardiovascular events in IMIDs. Data were pooled using fixed-effects or random-effects meta-analysis according to I(2) and pooled hazard ratios (HRs) and 95 % confidence intervals (CIs) were used as summary statistic. RESULTS: Our meta-analysis included 12 studies that comprised 148,722 patients with IMIDs (57,670 statin users, 91,052 statin non-users) contributing more than 840,113 patient-years. In pooled analysis, statin initiation was associated with 28 % decreased risk of all-cause mortality (random-effects: meta-HR 0.72, 95 % CI 0.65-0.80), 23 % decreased risk of major adverse cardiovascular events (fixed-effects: meta-HR 0.72, 95 % CI 0.62-0.83). Subgroup analysis of patients with rheumatoid arthritis showed similar results (fixed-effects: meta-HR 0.77, 95 % CI 0.67-0.89 for all-cause mortality; meta-HR 0.75, 95 % CI 0.63-0.88 for major adverse cardiovascular events). Furthermore, the protective role of statin in decreasing mortality was stronger in patients receiving statin for primary prevention of cardiovascular diseases than that

for secondary prevention (fixed-effects: meta-HR 0.64, 95 % CI 0.59-0.70; meta-HR 0.84, 95 % CI 0.80-0.89, respectively), although both were statistically significant. Additional analysis yielded similar benefit from statin usage between females and males regarding mortality. CONCLUSION: Statin use was associated with lower risks of mortality and cardiovascular events, with greater benefits for primary prevention in those IMIDs patients without prior cardiovascular disease.

[46] *Gün E, Uzun H, Bolu S et al.* **Serum 25-hydroxyvitamin D is associated with insulin resistance independently of obesity in children ages 5-17**. Prim Care Diabetes 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32616391
ABSTRACT
AIM: To determine the association of vitamin D with insulin resistance and obesity in children. METHODS: A total of 92 obese and 58 non-obese children aged 5-17 years were evaluated. Data were collected related to anthropometric (weight, height), and biochemical parameters (fasting plasma glucose, serum insulin, serum 25-hydroxyvitamin D, lipid profile, vitamin B12, parathormone) and physical examination (blood pressure, acanthosis nigricans, stria, lipomastia). Insulin resistance (IR) was calculated using the homeostasis model assessment (HOMA). HOMA-IR = fasting insulin level (μU/ml) × fasting glucose (mg/dL)/405. A HOMA-IR value >2.5 was defined as insulin resistance. RESULTS: According to the US Endocrine Society classification, vitamin D deficiency (0-20 ng/ml) was determined at significantly higher rates in the obese group than in the control group ($p < 0.001$). The rate of subjects with a vitamin D level of 20-30 ng/ml was significantly lower in the obese group than in the control group ($p < 0.001$) Within the obese group a statistically significant difference was determined between the insulin resistant and non-insulin resistant groups in respect of serum 25-hydroxyvitamin D levels ($p = 0.001$) and vitamin B12 levels ($p = 0.001$). A significant negative correlation was determined between serum 25-hydroxyvitamin D and HOMA-IR ($r=-0.256$, $p = 0.016$) and insulin ($r = -0.258$, $p = 0.015$). The systolic blood pressure ($p = 0.001$) and diastolic blood pressure ($p = 0.003$) values were significantly different in the control and obese groups. A statistically significant difference was determined between the control and obese groups in terms of the levels of insulin, HOMA-IR, HbA1c, cortisol, LDL, total cholesterol, HDL, triglyceride, hemoglobin, MCV, MPV, and calcium. CONCLUSION: The prevalence of vitamin D deficiency was higher in obese children compared to normal-weight and overweight children. Serum 25(OH)D levels showed a negative correlation with insulin and HOMA-IR. Serum 25(OH)D is associated with insulin resistance independently of obesity.

[47] *Shchinova AM, Shlevkova GV, Filatova AY et al.* **[Preprocedural high - sensitivity C-reactive protein (hsCRP) decrease during intensive atorvastatin therapy: the presumable impact on atherosclerosis progression after coronary stenting]**. Terapevticheskii arkhiv 2019; 91:10-15.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32598808
ABSTRACT
Proinflammatory status is the risk factor for coronary atherosclerosis progression after coronary stenting (CS). Intensive statin treatment is associated with hsCRP concentration decline. AIM: to evaluate prognostic significance of preprocedural hsCRP level reduction with intensive statin regimen for coronary atherosclerosis progression during one year after CS. MATERIALS AND METHODS: We enrolled 102 patients with stable angina who were on list

for scheduled CS. Group I (n=37) patients received atorvastatin 80 mg for 7 days before and 3 months after CS with further dose adjustment according to LDL; group II (n=65) patients received atorvastatin 20-40 mg/day for LDL goal achievement. HsCRP level was assessed at baseline, before CS and after 1, 3, 6 and 12 months. Coronary atherosclerosis progression was defined as new ≥50% stenosis or ≥30% increase of ≥20% pre - existing stenosis according to coronary angiography (CA) 1 year after CS. RESULTS: Baseline concentration of hsCRP was comparable: 0.21 (0.13; 0.38) vs. 0.20 (0.1; 0.44) mg/dl in groups I and II, respectively (p>0.05). In group I significant hsCRP level decrease to 0.14 (0.07; 0.32) mg/dl (p.

[48] *Zakharov AS, Michurova MS, Terekhin SA et al.* **[Intravascular ultrasound with virtual histology in assessment of atherosclerotic plaque composition in patients with coronary artery disease and type 2 diabetes mellitus]**. Terapevticheskii arkhiv 2019; 91:41-46.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32598588
ABSTRACT
Type 2 diabetes mellitus (T2DM) is a serious medical and social problem leading to early disability of patients and high mortality from cardiovascular complications. The development of cardiovascular events is associated not only with the degree of coronary artery stenosis, but also with the structure of the atherosclerotic plaque. AIM: This study aimed to characterize structure and composition of coronary artery atherosclerotic plaque in target lesion of T2DM patients and patients without diabetes using intravascular ultrasound (IVUS) and IVUS with virtual histology (IVUS-VH). MATERIALS AND METHODS: We observed 25 patients with coronary artery disease (CAD) with T2DM and without T2DM, which admitted to Endocrinology Research Centre to perform percutaneous coronary intervention (PCI). Patients with CAD and T2DM were included at group 1 and patients with CAD and without T2DM were included at group 2. IVUS and IVUS-VH assessment of target lesion were performed prior to stent implantation. We observed 24 plaques at group 1 and 10 plaques at group 2. RESULTS: In grey - scale IVUS 2D analysis there were no differences in mean cross - sectional area of the vessel (12.5 [10.4; 15.8] mm2 vs. 13.5 [12,7; 16.5] mm2; p=0.223, respectively) and lumen area (3.71 [2.5; 4.5] mm2 vs. 3.2 [2.7; 3.8] mm2; p=0.589, respectively). Plaque burden were higher in patients without T2DM (71.6 [65.5; 75.7] % vs. 77.6 [74.4; 80.4] %; p=0.008, respectively). IVUS-VH analysis showed that percent of necrotic core and dense calcium areas were significantly higher in the T2DM group (31.3 [25.3; 36.5] % vs. 21.65 [14.3; 27.8] %; p=0.01 and 4.7 [2.3; 7.8] % vs. 2.45 [1.2; 4.05] %; p=0.046, respectively). Percent of the fibrotic tissue were higher in non-T2DM group (55.35 [49.7; 63.6] % vs 67.7 [61.8; 76.5] %; p=0.004, respectively). There were no differences in percent of lipidic tissue in both groups. CONCLUSIONS: IVUS-VH assessment of coronary artery atherosclerotic plaques showed greater amount of necrotic core and dense calcium in patients with T2DM compared to patients without diabetes.

[49] *Weitz JI, Angiolillo DJ, Geisler T, Heitmeier S*. **Dual Pathway Inhibition for Vascular Protection in Patients with Atherosclerotic Disease: Rationale and Review of the Evidence**. Thrombosis and haemostasis 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32594508
ABSTRACT

Literature update week 27 (2020)

Despite advances in secondary prevention strategies in patients with cardiovascular disease, the residual risk of recurrent atherothrombotic events remains high. Dual-antiplatelet therapy is the standard of care for secondary prevention in patients with acute coronary syndrome (ACS), whereas single antiplatelet therapy, generally with aspirin, is the standard of care for secondary prevention in stable patients with coronary artery disease (CAD), peripheral artery disease (PAD), or cerebrovascular disease. However, atherosclerotic plaque disruption not only triggers platelet activation but also results in thrombin generation because of tissue factor exposure. Therefore, blocking both pathways by combining antiplatelet therapy with an anticoagulant, or dual pathway inhibition (DPI), has the potential to be more effective than inhibiting either pathway alone. The benefit of DPI has been demonstrated in the ATLAS ACS 2-TIMI 51, COMPASS, and VOYAGER PAD trials, where the combination of rivaroxaban vascular dose (2.5 mg twice daily) plus aspirin significantly reduced the risk of atherothrombotic events compared with aspirin across a broad range of patients, including those with recent ACS, those with chronic CAD and/or PAD, and patients with PAD who have undergone peripheral revascularization. This article provides the rationale for this regimen in more detail, including why the DPI regimen with the rivaroxaban vascular dose was developed for vascular protection in a broad spectrum of patients with atherosclerotic disease.