Literature update week 11 (2020)

[1] *Chatterjee S, Hajra A, Bandyopadhyay D et al.* **Defining the Role of Icosapent Ethyl in Clinical Practice**. American journal of cardiovascular drugs : drugs, devices, and other interventions 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32157567
ABSTRACT
The health benefit of fish oil, i.e. omega-3 fatty acids (omega-3 FA) has a long history of debate. While there are a number of medications to reduce serum triglyceride levels, none have shown unanimous cardiovascular (CV) benefits. The most recent Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention Trial (REDUCE-IT) assessing the CV outcome of one highly purified prescription omega-3 FA has certainly rejuvenated the debate. While this trial has been regarded as one of the most important landmark trials in preventive cardiology, the tolerability issue in a very high dose (4 g/day, as administered in the trial) is still a matter of concern. This article summarizes the current status and future perspective of icosapent ethyl in clinical practice in light of REDUCE-IT.

[2] *Hamilton D, Sr., Nandkeolyar S, Lan H et al.* **Amiodarone: A Comprehensive Guide for Clinicians**. American journal of cardiovascular drugs : drugs, devices, and other interventions 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32166725
ABSTRACT
Amiodarone is an effective antiarrhythmic medication frequently used in practice for both ventricular and atrial arrhythmias. Though classified as a class III antiarrhythmic, it affects all phases of the cardiac action potential. However, the drug has several side effects, including thyroid abnormalities, pulmonary fibrosis, and transaminitis, for which routine monitoring is recommended. It also interacts with several medications, such as warfarin, simvastatin, and atorvastatin, and many HIV antiretroviral medications. Given the common use of this medication in medical practice, it is vital that clinicians understand the indications, contraindications, dosing, side effects, and interactions of this medication. A thorough understanding of these topics is essential for clinicians to ensure safe and effective use of amiodarone.

[3] *Niman S, Rana K, Reid J et al.* **A Review of the Efficacy and Tolerability of Bempedoic Acid in the Treatment of Hypercholesterolemia**. American journal of cardiovascular drugs : drugs, devices, and other interventions 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32166726
ABSTRACT
Despite the widespread use of statins and ezetimibe to decrease low-density lipoprotein cholesterol (LDL-C) levels and associated atherosclerotic cardiovascular disease (ASCVD), many patients do not achieve adequate LDL-C lowering as per the recommended American College of Cardiology (ACC)/American Heart Association (AHA) and European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS) guidelines and demonstrate residual cardiovascular risk. The introduction of proprotein convertase subtilisin/kexin type 9 (PCSK-9) inhibitors in 2015 was a promising addition to hypercholesterolemia therapies, but their cost and subcutaneous administration has limited their use, and therefore, new affordable and patient friendly treatment strategies are crucial to help reduce ASCVD risk. Bempedoic acid, a drug currently under investigation, is a small molecule that has been shown to upregulate LDL receptors, decrease LDL-C, and reduce atherosclerotic plaque formation in hypercholesterolemic patients. Furthermore, bempedoic acid is a prodrug that becomes activated by an enzyme expressed primarily in the liver, allowing it to avoid the potential myotoxicity associated

with statin therapy. The purpose of this review is to summarize the major clinical studies evaluating bempedoic acid and describe its potential addition to currently approved lipid-lowering therapies.

[4] *Jiang P, Chen Z, Hippe DS et al.* **Association Between Carotid Bifurcation Geometry and Atherosclerotic Plaque Vulnerability: A Chinese Atherosclerosis Risk Evaluation Study**. Arteriosclerosis, thrombosis, and vascular biology 2020:Atvbaha119313830.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32160772
ABSTRACT
OBJECTIVE: Carotid bifurcation geometry has been believed to be a risk factor for the initiation of atherosclerosis because of its in fl uence on hemodynamics. However, the relationships between carotid bifurcation geometry and plaque vulnerability are not fully understood. This study aimed to determine the association between carotid bifurcation geometry and plaque vulnerability using magnetic resonance vessel wall imaging. Approach and Results: A total of 501 carotid arteries with nonstenotic atherosclerosis were included from the cross-sectional, multicenter CARE II study (Chinese Atherosclerosis Risk Evaluation). Four standardized carotid bifurcation geometric parameters (bifurcation angle, internal carotid artery planarity, luminal expansion FlareA, and tortuosity Tort2D) were derived from time-of-flight magnetic resonance imaging. Presence of vulnerable plaque, which has intraplaque hemorrhage, large lipid-rich necrotic core, or disrupted luminal surface, was determined based on multicontrast carotid magnetic resonance vessel wall images. Vulnerable plaques (N=43) were found to occur at more distal locations (ie, near the level of flow divider) than stable plaques (N=458). Multivariable logistic regression shows that the luminal expansion FlareA (odds ratio, 0.45 [95% CI, 0.25-0.81]; P=0.008) was associated with plaque vulnerability after adjustment for age, sex, maximum wall thickness, plaque location, and other geometric parameters. CONCLUSIONS: Smaller luminal expansion at carotid bifurcation is associated with vulnerable plaque. The finding needs to be verified with longitudinal studies and the underlying mechanism should be further explored with hemodynamics measurement in the future.

[5] *Ruhanen H, Haridas PAN, Minicocci I et al.* **ANGPTL3 deficiency alters the lipid profile and metabolism of cultured hepatocytes and human lipoproteins**. Biochimica et biophysica acta. Molecular and cell biology of lipids 2020; 1865:158679.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32151767
ABSTRACT
Loss-of-function (LOF) mutations in ANGPTL3, an inhibitor of lipoprotein lipase (LPL), cause a drastic reduction of serum lipoproteins and protect against the development of atherosclerotic cardiovascular disease. Therefore, ANGPTL3 is a promising therapy target. We characterized the impacts of ANGPTL3 depletion on the immortalized human hepatocyte (IHH) transcriptome, lipidome and human plasma lipoprotein lipidome. The transcriptome of ANGPTL3 knock-down (KD) cells showed altered expression of several pathways related to lipid metabolism. Accordingly, ANGPTL3 depleted IHH displayed changes in cellular overall fatty acid (FA) composition and in the lipid species composition of several lipid classes, characterized by abundant n-6 and n-3 polyunsaturated FAs (PUFAs). This PUFA increase coincided with an elevation of lipid mediators, among which there were species relevant for resolution of inflammation, protection from lipotoxic and hypoxia-induced ER stress, hepatic steatosis and insulin resistance or for the recovery from cardiovascular events. Cholesterol esters were markedly reduced in ANGPTL3 KD IHH, coinciding with suppression of the SOAT1 mRNA and protein. ANGPTL3 LOF caused

alterations in plasma lipoprotein FA and lipid species composition. All lipoprotein fractions of the ANGPTL3 LOF subjects displayed a marked drop of 18:2n-6, while several highly unsaturated triacylglycerol (TAG) species were enriched. The present work reveals distinct impacts of ANGPTL3 depletion on the hepatocellular lipidome, transcriptome and lipid mediators, as well as on the lipidome of lipoproteins isolated from plasma of ANGPTL3-deficient human subjects. It is important to consider these lipidomics and transcriptomics findings when targeting ANGPTL3 for therapy and translating it to the human context.

[6] *van der Sluis RJ, Depuydt MAC, Van Eck M, Hoekstra M*. **VLDL/LDL serves as the primary source of cholesterol in the adrenal glucocorticoid response to food deprivation**. Biochimica et biophysica acta. Molecular and cell biology of lipids 2020; 1865:158682.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32169652
ABSTRACT
The contribution of individual lipoprotein species to the generation of the adrenal cholesterol pool used for the synthesis of anti-inflammatory glucocorticoid species remains unknown. Here we examined the impact of specific lowering of very low-density lipoprotein (VLDL) and low-density (LDL) levels on adrenal cholesterol and glucocorticoid homeostasis. Hereto, lethally-irradiated hypercholesterolemic apolipoprotein E (APOE) knockout mice received APOE-containing bone marrow from wild-type mice (n = 6) or APOE knockout control bone marrow (n = 10) and were subsequently fed a regular chow diet. Transplantation with wild-type bone marrow was associated with a 10-fold decrease in VLDL/LDL-cholesterol levels. No changes were observed in adrenal weights, adrenal cholesterol content, or basal plasma corticosterone levels. However, food deprivation-induced corticosterone secretion was 64% lower ($P < 0.05$) in wild-type bone marrow recipients as compared to APOE knockout bone marrow recipients, in the context of similar plasma adrenocorticotropic hormone (ACTH) levels. A parallel 19-29% decrease in adrenal relative mRNA expression levels of ACTH-responsive genes SR-BI ($P < 0.01$), STAR ($P < 0.05$), and CYP11A1 ($P < 0.05$) was detected. In support of relative glucocorticoid insufficiency, blood lymphocyte and eosinophil concentrations were respectively 2.4-fold ($P < 0.01$) and 8-fold ($P < 0.001$) higher in wild-type bone marrow recipients under food deprivation stress conditions. In conclusion, we have shown that a selective lowering of VLDL/LDL levels in APOE knockout mice through a transplantation with APOE-containing wild-type bone marrow is associated with a decreased maximal adrenal glucocorticoid output. Our studies provide experimental support for the hypothesis that, in vivo, VLDL/LDL serves as the primary source of cholesterol used for glucocorticoid synthesis during food deprivation stress.

[7] *Liu HW, Luo Y, Zhou YF, Chen ZP*. **Probucol Prevents Diabetes-Induced Retinal Neuronal Degeneration through Upregulating Nrf2**. BioMed research international 2020; 2020:3862509.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32149102
ABSTRACT
Diabetic retinopathy (DR) is a sight-threatening complication of diabetes. This study investigated the therapeutic effect of probucol in a mouse model of diabetic retinopathy. C57BL/6 mice were rendered diabetic through Streptozotocin (STZ) intraperitoneal injection. Mice were treated with probucol (150 mg/kg, gavage administration) or vehicle (DMSO) for 12 weeks. Optical coherence tomography (OCT), fundus photography (FP), and fundus fluorescein angiography (FFA) were conducted to evaluate retinal structure and damage. Eyes were collected for histology, reactive oxygen species (ROS) assay,

apoptotic cells count, and western blot. After STZ injection, all mice developed hyperglycemia. Compared with the retina of the control group, the retina of diabetic mice showed enhanced arterial reflex and beaded vein dilatation. Besides, reduced inner and middle retinal thickness and significantly fewer nuclei were found in diabetic retina. Moreover, the diabetic retina also presented increased ROS generation and more TUNEL-positive cells. Probucol treatment prevented diabetes-induced lesions. In addition, the treatment also upregulated Nrf2 expression in diabetic retina. It was suggested that probucol attenuated diabetes-induced retinal neuronal degeneration via upregulating the Nrf2 signaling pathway possibly. Probucol may be repurposed for DR management.

[8] *Costantine MM*. **Author's reply re: Pravastatin to ameliorate early onset pre-eclampsia: promising but not there yet**. BJOG : an international journal of obstetrics and gynaecology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32154980
ABSTRACT

[9] *Olesen TB, Pareek M, Stidsen JV et al.* **Association between antecedent blood pressure, hypertension-mediated organ damage and cardiovascular outcome**. Blood pressure 2020:1-9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32157916
ABSTRACT
Purpose: The objective of this study was to test if combining antecedent systolic blood pressure (SBP) with traditional risk factors and hypertension-mediated organ damage (HMOD) improves risk stratification for subsequent cardiovascular disease.Materials and methods: 1910 subjects participated in this study. Antecedent SBP was defined as the average of measurements obtained in 1982 and in 1987. Current SBP was obtained in 1993. HMOD were examined in 1993. HMOD was defined as either atherosclerotic plaque(s), increased pulse wave velocity, increased urine albumin creatinine ratio (above the 90th percentile) or left ventricular hypertrophy. Major adverse cardiovascular events (MACE) including myocardial infarction, cerebrovascular disease, heart failure and arrhythmia were obtained from national registries.Results: Subjects were divided into two age categories: a middle-aged group (aged 41 or 51) and an older group (aged 61 or 71). From 1993 to 2010, 425 events were observed. In multivariable analysis with both current and antecedent SBP adjusted for traditional risk factors, current SBP was associated with each measure of HMOD whilst antecedent SBP was not significantly associated with urine albumin creatinine ratio in the older group, LVMI in the middle-aged group, or the presence of plaque in any of the age groups (all $p > 0.15$). When current and antecedent SBP were evaluated together, current SBP was not associated with MACE in the middle-aged subgroup [HR = 1.09 (0.96-1.22), $p = 0.18$] but remained associated with MACE in the older subgroup [HR = 1.21 (1.10-1.34), $p < 0.01$]. Contrariwise, antecedent SBP was only associated with MACE in the middle-aged subgroup [HR = 1.24 (1.04-1.48), $p = 0.02$]. Adding antecedent SBP to traditional risk factors did not improve the predictive accuracy of the survival model.Conclusion: In healthy non-medicated middle-aged subjects, antecedent SBP is associated with cardiovascular outcome independently of current BP, traditional risk factors and HMOD. However, improvement in risk stratification seems to be limited.

[10] *Christou GA, Mprikos SG, Christou KA et al.* **High Tolerability of Pitavastatin Therapy: A Case Report of Comparison with other Statins**. Cardiology 2020:1-4.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32160627
ABSTRACT

INTRODUCTION: Myopathy is possibly the most clinically relevant statin-induced side effect. CASE PRESENTATION: We report a case of a 63-year-old healthy male with mixed dyslipidemia. He developed bilateral myalgia of the forearms with fluvastatin 40 mg/day, pravastatin 20 mg/day, and combination of atorvastatin 10 mg and ezetimibe 10 mg/day. The only hypolipidemic treatment that was tolerable was the combination of pitavastatin 1 mg and ezetimibe 10 mg/day. DISCUSSION: Pitavastatin demonstrated less potential for the development of myalgia compared to the so far considered most tolerable statins (i.e., fluvastatin and pravastatin). All the tested statins were used at the lowest approved dose for clinical use. CONCLUSION: The combination of pitavastatin 1 mg and ezetimibe appears to be a promising treatment choice for individuals who are intolerant to statin therapy due to muscle complaints.

[11] *Tang Y, Li SL, Hu JH et al.* **Research progress on alternative non-classical mechanisms of PCSK9 in atherosclerosis in patients with and without diabetes**. Cardiovascular diabetology 2020; 19:33.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32169071
ABSTRACT
The proprotein convertase subtilisin/kexin type 9 (PCSK9) acts via a canonical pathway to regulate circulating low-density lipoprotein-cholesterol (LDL-C) via degradation of the LDL receptor (LDLR) on the liver cell surface. Published research has shown that PCSK9 is involved in atherosclerosis via a variety of non-classical mechanisms that involve lysosomal, inflammatory, apoptotic, mitochondrial, and immune pathways. In this review paper, we summarized these additional mechanisms and described how anti-PCSK9 therapy exerts effects through these mechanisms. These additional pathways further illustrate the regulatory role of PCSK9 in atherosclerosis and offer an in-depth interpretation of how the PCSK9 inhibitor exerts effects on the treatment of atherosclerosis.

[12] *Hartley MD, Shokat MD, DeBell MJ et al.* **Pharmacological Complementation Remedies an Inborn Error of Lipid Metabolism**. Cell chemical biology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32169163
ABSTRACT
X-linked adrenoleukodystrophy (X-ALD) is a rare, genetic disease in which increased very long chain fatty acids (VLCFAs) in the central nervous system (CNS) cause demyelination and axonopathy, leading to neurological deficits. Sobetirome, a potent thyroid hormone agonist, has been shown to lower VLCFAs in the periphery and CNS. In this study, two pharmacological strategies for enhancing the effects of sobetirome were tested in Abcd1 KO mice, a murine model with the same inborn error of metabolism as X-ALD patients. First, a sobetirome prodrug (Sob-AM2) with increased CNS penetration lowered CNS VLCFAs more potently than sobetirome and was better tolerated with reduced peripheral exposure. Second, co-administration of thyroid hormone with sobetirome enhanced VLCFA lowering in the periphery but did not produce greater lowering in the CNS. These data support the conclusion that CNS VLCFA lowering in Abcd1 knockout mice is limited by a mechanistic threshold related to slow lipid turnover.

[13] *Kim YS, Kim JK, Hanh BTB et al.* **The Peroxisome Proliferator-Activated Receptor alpha- Agonist Gemfibrozil Promotes Defense Against Mycobacterium abscessus Infections**. Cells 2020; 9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32155958
ABSTRACT

Peroxisome proliferator-activated receptor alpha (PPARalpha) shows promising potential to enhance host defenses against Mycobacterium tuberculosis infection. Herein we evaluated the protective effect of PPARalpha against nontuberculous mycobacterial (NTM) infections. Using a rapidly growing NTM species, Mycobacterium abscessus (Mabc), we found that the intracellular bacterial load and histopathological damage were increased in PPARalpha-null mice in vivo. In addition, PPARalpha deficiency led to excessive production of proinflammatory cytokines and chemokines after infection of the lung and macrophages. Notably, administration of gemfibrozil (GEM), a PPARalpha activator, significantly reduced the in vivo Mabc load and inflammatory response in mice. Transcription factor EB was required for the antimicrobial response against Mabc infection. Collectively, these results suggest that manipulation of PPARalpha activation has promising potential as a therapeutic strategy for NTM disease.

[14] *Hou ZH, Lu B, Li ZN et al.* **Quantification of atherosclerotic plaque volume in coronary arteries by computed tomographic angiography in subjects with and without diabetes**. Chinese medical journal 2020; 133:773-778.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32149765
ABSTRACT
BACKGROUND: Diabetes mellitus (DM) is considered a cardiovascular risk factor. The aim of this study was to analyze the prevalence and volume of coronary artery plaque in patients with diabetes mellitus (DM) vs. those without DM. METHODS: This study recruited consecutive patients who underwent coronary computed tomography (CT) angiography (CCTA) between October 2016 and November 2017. Personal information including conventional cardiovascular risk factors was collected. Plaque phenotypes were automatically calculated for volume of different component. The volume of different plaque was compared between DM patients and those without DM. RESULTS: Among 6381 patients, 931 (14.59%) were diagnosed with DM. The prevalence of plaque in DM subjects was higher compared with nondiabetic group significantly (48.34% vs. 33.01%, chi = 81.84, P < 0.001). DM was a significant risk factor for the prevalence of plaque in a multivariate model (odds ratio [OR] = 1.465, 95% CI: 1.258-1.706, P < 0.001). The volume of total plaque and any plaque subtypes in the DM subjects was greater than those in nondiabetic patients significantly (P < 0.001). CONCLUSION: The coronary artery atherosclerotic plaques were significantly higher in diabetic patients than those in non-diabetic patients.

[15] *Evans NR, Tarkin JM, Chowdhury MM et al.* **Dual-Tracer Positron-Emission Tomography for Identification of Culprit Carotid Plaques and Pathophysiology In Vivo**. Circulation. Cardiovascular imaging 2020; 13:e009539.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32164454
ABSTRACT
BACKGROUND: Inflammation and microcalcification are interrelated processes contributing to atherosclerotic plaque vulnerability. Positron-emission tomography can quantify these processes in vivo. This study investigates (1) (18)F-fluorodeoxyglucose (FDG) and (18)F-sodium fluoride (NaF) uptake in culprit versus nonculprit carotid atheroma, (2) spatial distributions of uptake, and (3) how macrocalcification affects this relationship. METHODS: Individuals with acute ischemic stroke with ipsilateral carotid stenosis of >/=50% underwent FDG-positron-emission tomography and NaF-positron-emission tomography. Tracer uptake was quantified using maximum tissue-to-background

ratios (TBRmax) and macrocalcification quantified using Agatston scoring. RESULTS: In 26 individuals, median most diseased segment TBRmax (interquartile range) was higher in culprit than in nonculprit atheroma for both FDG (2.08 [0.52] versus 1.89 [0.40]; P<0.001) and NaF (2.68 [0.63] versus 2.39 [1.02]; P<0.001). However, whole vessel TBRmax was higher in culprit arteries for FDG (1.92 [0.41] versus 1.71 [0.31]; P<0.001) but not NaF (1.85 [0.28] versus 1.79 [0.60]; P=0.10). NaF uptake was concentrated at carotid bifurcations, while FDG was distributed evenly throughout arteries. Correlations between FDG and NaF TBRmax differed between bifurcations with low macrocalcification (rs=0.38; P<0.001) versus high macrocalcification (rs=0.59; P<0.001). CONCLUSIONS: This is the first study to demonstrate increased uptake of both FDG and NaF in culprit carotid plaques, with discrete distributions of pathophysiology influencing vulnerability in vivo. These findings have implications for our understanding of the natural history of the disease and for the clinical assessment and management of carotid atherosclerosis.

[16] *Ridker PM*. **From CANTOS to CIRT to COLCOT to Clinic: Will All Atherosclerosis Patients Soon Be Treated With Combination Lipid-Lowering and Inflammation-Inhibiting Agents?** Circulation 2020; 141:787-789.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32150469
ABSTRACT

[17] *Alothman L, Zawadka M, Aljenedil S et al.* **Prediction of Familial Hypercholesterolemia in Patients at High Atherosclerotic Cardiovascular Disease Risk Using a Recently Validated Algorithm**. CJC Open 2019; 1:190-197.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32159106
ABSTRACT
Background: The prevalence of heterozygous familial hypercholesterolemia (FH) is 1 of 250 in the general population and approximately 1 of 125 in patients with atherosclerotic cardiovascular disease (ASCVD), yet only a minority are diagnosed. The diagnostic criteria for FH rely on a point system using low-density lipoprotein cholesterol (LDL-C), family history, cutaneous manifestations, and molecular diagnosis. The aim of the present study was to determine the prevalence of FH in the Relating Evidence to Achieve Cholesterol Targets (REACT) registry. Methods: Patients were enrolled as ASCVD (n = 86) or FH (n = 109) and with an LDL-C level > 3.0 mmol/L despite maximally tolerated statin therapy. FH was diagnosed clinically using a validated clinical application integrating an imputation for baseline (untreated) LDL-C levels. Results: There were 109 men and 86 women with a mean age of 63 +/- 12 years. Diabetes (29.7%), hypertension (62.1%), smoking (37.9%), and family history of premature ASCVD (59.5%) were common. On-treatment LDL-C was 4.26 +/- 0.94 mmol/L. On the basis of the dose and type of statin +/- ezetimibe, imputed baseline LDL-C was 7.04 +/- 2.90 mmol/L. A diagnosis of probable/definite FH was found in 54.7%, 49.5%, and 61.5% of patients according to the Simon Broome, Dutch Lipid Clinic Network criteria, and the new Canadian FH definition, respectively. Of note, 40% of patients in the ASCVD inclusion subgroup had probable or definite FH. Conclusions: Our study reveals that a substantial proportion of patients with ASCVD whose LDL-C levels are > 3.0 mmol/L despite maximally tolerated statins have heterozygous FH. Clinicians should consider using the recently described algorithm to assess the possibility of FH in this high-risk population.

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[18] *Zhang J, Wang J, Yu H et al.* **Comparison between atorvastatin and rosuvastatin on secondary percutaneous coronary intervention rate and the risk factors in patients with coronary heart disease**. Current drug metabolism 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32156233
ABSTRACT
Background Statins are effective for patients in decreased low-density lipoprotein therapy. Objective We wanted to compare atorvastatin versus rosuvastatin on secondary percutaneous coronary intervention (PCI) rate and explore risk factors in coronary heart disease (CHD) patients. Methods A cohort study with 283 CHD subjects was launched from 2011 to 2015. Cox proportional hazards regression model, Receiver Operating Characteristic (ROC) and nomogram were used to compare effect of atorvastatin and rosuvastatin on secondary PCI rate and disease risk factors. Even, we explored that why the two statins had different effects based on gene expression profile analysis. Results Gene FFA (Freely fatty acid), AST (Aspartate Transaminase) and ALT (Alanine transaminase) showed the statistical difference between the four statin groups (P<0.05). In AA group (Continuous Atorvastatin usage), albumin was a risk factor (Hazard Ratio (HR):1.076, 95%CI (1.001, 1.162), p<0.05). In AR group (Start with Atorvastatin usage, then change to Rosuvastatin usage), ApoA was a protective factor (HR:0.004, 95%CI (0.001, 0.665), p<0.05). GLB (Galactosidase Beta) was a risk factor (HR:1.262, 95%CI (1.010, 1.576), p<0.05). In RR group (Continuous Rosuvastatin usage), ApoE was a protective factor (HR:0.943, 95%CI (0.890, 1.000), p<0.05). ALT was a risk factor (HR:1.030, 95%CI (1.000, 1.060), p<0.05). Conclusion Patients in RA group the lowest secondary PCI rate. ALT was a risk factor in RR group. Gene Gpt (Glutamic Pyruvic Transaminase) encoded for one subtype of ALT was significantly different expression in different statin groups.

[19] *van der Meij BS, Mazurak VC*. **Fish oil supplementation and maintaining muscle mass in chronic disease: state of the evidence**. Current opinion in clinical nutrition and metabolic care 2020; 23:164-173.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32167986
ABSTRACT
PURPOSE OF REVIEW: Providing eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), in the form of fish oils, to benefit muscle is an emerging area of interest. The aim of this work was to evaluate the current literature that has assessed muscle mass as an outcome during a fish oil intervention in any chronic disease. RECENT FINDINGS: The vast majority of studies published in the last 3 years (12 of 15) have been conducted in the oncological setting, in patients undergoing treatment for cancers of the gastrointestinal tract, breast, head and neck, lung, cervix, and hematological cancers. Three studies were conducted in patients with chronic obstructive pulmonary disease (COPD). Fish oil was provided as part of nutrient mixtures in 12 studies and as capsules in three studies. SUMMARY: Overall, the evidence for an effect of fish oil supplementation on muscle mass in patients with cancer undergoing treatment and in COPD remains unequivocal and reveals limited new knowledge in the area of fish oil supplementation in the cancer setting. Recent literature continues to provide mixed evidence on the efficacy of fish oil on muscle mass and function. The present review highlights challenges in comparing and interpreting current studies aimed at testing fish oil supplementation for muscle health.

[20] *Dharmalingam M, Aravind SR, Thacker H et al.* **Efficacy and Safety of Remogliflozin Etabonate, a New Sodium Glucose Co-Transporter-2 Inhibitor, in Patients with Type 2 Diabetes Mellitus: A 24-Week, Randomized, Double-Blind, Active-Controlled Trial**. Drugs 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32162274
ABSTRACT
BACKGROUND: Metformin is the first-line treatment for type 2 diabetes mellitus (T2DM), but many patients either cannot tolerate it or cannot achieve glycemic control with metformin alone, so treatment with other glucose-lowering agents in combination with metformin is frequently required. Remogliflozin etabonate, a novel agent, is an orally bioavailable prodrug of remogliflozin, which is a potent and selective sodium-glucose co-transporter-2 inhibitor. OBJECTIVE: Our objective was to evaluate the efficacy and safety of remogliflozin etabonate compared with dapagliflozin in subjects with T2DM in whom a stable dose of metformin as monotherapy was providing inadequate glycemic control. METHODS: A 24-week randomized, double-blind, double-dummy, active-controlled, three-arm, parallel-group, multicenter, phase III study was conducted in India. Patients aged >/= 18 and </= 65 years diagnosed with T2DM, receiving metformin >/= 1500 mg/day, and with glycated hemoglobin (HbA1c) levels >/= 7 to </= 10% at screening were randomized into three groups. Every patient received metformin >/= 1500 mg and either remogliflozin etabonate 100 mg twice daily (BID) (group 1, n = 225) or remogliflozin etabonate 250 mg BID (group 2, n = 241) or dapagliflozin 10 mg once daily (QD) in the morning and placebo QD in the evening (group 3, n = 146). The patients were followed-up at weeks 1 and 4 and at 4-week intervals thereafter until week 24. The endpoints included mean change in HbA1c (primary endpoint, noninferiority margin = 0.35), fasting plasma glucose (FPG), postprandial plasma glucose (PPG), bodyweight, blood pressure, and fasting lipids. Treatment-emergent adverse events (TEAEs), safety laboratory values, electrocardiogram, and vital signs were evaluated. RESULTS: Of 612 randomized patients, 167 (group 1), 175 (group 2), and 103 (group 3) patients with comparable baseline characteristics completed the study. Mean change +/- standard error (SE) in HbA1c from baseline to week 24 was - 0.72 +/- 0.09, - 0.77 +/- 0.09, and - 0.58 +/- 0.12% in groups 1, 2, and 3, respectively. The difference in mean HbA1c of group 1 versus group 3 (- 0.14%, 90% confidence interval [CI] - 0.38 to 0.10) and group 2 versus group 3 (- 0.19%; 90% CI - 0.42 to 0.05) was noninferior to that in group 3 ($p < 0.001$). No significant difference was found between group 1 or group 2 and group 3 in change in FPG, PPG, and bodyweight. The overall incidence of TEAEs was comparable across study groups (group 1 = 32.6%, group 2 = 34.4%, group 3 = 29.5%), including adverse events (AEs) of special interest (hypoglycemic events, urinary tract infection, genital fungal infection). Most TEAEs were mild to moderate in intensity, and no severe AEs were reported. CONCLUSION: This study demonstrated the noninferiority of remogliflozin etabonate 100 and 250 mg compared with dapagliflozin, from the first analysis of an initial 612 patients. Remogliflozin etabonate therefore may be considered an effective and well-tolerated alternative treatment option for glycemic control in T2DM. TRIAL REGISTRATION: CTRI/2017/07/009121.

[21] *Kim AS, Hakeem R, Abdullah A et al.* **Therapeutic plasma exchange for the management of severe gestational hypertriglyceridaemic pancreatitis due to lipoprotein lipase mutation**. Endocrinology, diabetes & metabolism case reports 2020; 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32168469
ABSTRACT

Literature update week 11 (2020)

Summary: A 19-year-old female presented at 25-weeks gestation with pancreatitis. She was found to have significant hypertriglyceridaemia in context of an unconfirmed history of familial hypertriglyceridaemia. This was initially managed with fasting and insulin infusion and she was commenced on conventional interventions to lower triglycerides, including a fat-restricted diet, heparin, marine oil and gemfibrozil. Despite these measures, the triglyceride levels continued to increase as she progressed through the pregnancy, and it was postulated that she had an underlying lipoprotein lipase defect. Therefore, a multidisciplinary decision was made to commence therapeutic plasma exchange to prevent further episodes of pancreatitis. She underwent a total of 13 sessions of plasma exchange, and labour was induced at 37-weeks gestation in which a healthy female infant was delivered. There was a rapid and significant reduction in triglycerides in the 48 h post-delivery. Subsequent genetic testing of hypertriglyceridaemia genes revealed a missense mutation of the LPL gene. Fenofibrate and rosuvastatin was commenced to manage her hypertriglyceridaemia postpartum and the importance of preconception counselling for future pregnancies was discussed. Hormonal changes in pregnancy lead to an overall increase in plasma lipids to ensure adequate nutrient delivery to the fetus. These physiological changes become problematic, where a genetic abnormality in lipid metabolism exists and severe complications such as pancreatitis can arise. Available therapies for gestational hypertriglyceridaemia rely on augmentation of LPL activity. Where there is an underlying LPL defect, these therapies are ineffective and removal of triglyceride-rich lipoproteins via plasma exchange should be considered. Learning points: Hormonal changes in pregnancy, mediated by progesterone,oestrogen and human placental lactogen, lead to a two- to three-fold increase in serum triglyceride levels. Pharmacological intervention for management of gestational hypertriglyceridaemia rely on the augmentation of lipoprotein lipase (LPL) activity to enhance catabolism of triglyceride-rich lipoproteins. Genetic mutations affecting the LPL gene can lead to severe hypertriglyceridaemia. Therapeutic plasma exchange (TPE) is an effective intervention for the management of severe gestational hypertriglyceridaemia and should be considered in cases where there is an underlying LPL defect. Preconception counselling and discussion regarding contraception is of paramount importance in women with familial hypertriglyceridaemia.

[22] *Peppas S, Piovani D, Peyrin-Biroulet L et al.* **Statins and inflammatory bowel disease: Where do we stand?** European journal of internal medicine 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32151491
ABSTRACT
Inflammatory bowel disease is a chronic autoimmune disorder of the western world that is rapidly expanding in newly industrialized countries. Novel strategies are urgently needed to prevent and improve the treatment of this costly and disabling disease. Statins are the most commonly prescribed drugs worldwide. Besides their lipid-lowering effects, statins may exert complex immunomodulatory properties and multiple pleiotropic effects including the inhibition of T-cell activation, antigen-presenting function and leukocyte infiltration of target organs which might render statins as beneficial agents for inflammatory and autoimmune conditions. In this review, we summarize the experimental findings on the topic, and critically appraise the epidemiological evidence regarding the value of statins as a potential strategy for preventing and treating inflammatory bowel disease. Several experimental studies have shown that statins reduce inflammation in animal models of colitis; however, clinical studies investigating their disease-modifying and preventive potential in IBD have demonstrated some limitations and conflicting results. The available epidemiological evidence is not yet sufficient to

support the use of statin for preventing or treating inflammatory bowel disease. Additional high-quality research is warranted.

[23] *Rao Y, Xu Z, Hu YT et al.* **Discovery of a promising agent IQZ23 for the treatment of obesity and related metabolic disorders**. European journal of medicinal chemistry 2020; 192:112172.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32163815
ABSTRACT
Discovery of novel anti-obesity agents is a challenging and promising research area. Based on our previous works, we synthesized 40 novel beta-indoloquinazoline analogues by altering the skeleton and introducing preferential side chains, evaluated their lipid-lowering activity and summarized the structure-activity relationships. In combination with an evaluation of the lipid-lowering efficacies, AMP-dependent activated protein kinase (AMPK) activating ability and liver microsomal stability, compound 23 (named as IQZ23) was selected for further studies. IQZ23 exerted a high efficacy in decreasing the triglyceride level (EC50 = 0.033 muM) in 3T3-L1 adipocytes. Mechanistic studies revealed the lipid-lowering activity of IQZ23 was dependent on the AMPK pathway by modulating ATP synthase activity. This activation was accompanied by mitochondrial biogenesis and oxidation capacity increased, and insulin sensitivity enhanced in pertinent cell models by various interventions. Correspondingly, IQZ23 (20 mg/kg, i.p.) treatment significantly reversed high fat and cholesterol diet (HFC)- induced body weight increases and accompanying clinical symptoms of obesity in mice but without indicative toxicity. These results indicate that IQZ23 could be a useful candidate for the treatment of obesity and related metabolic disorders.

[24] *Kwon MY, Hwang N, Back SH et al.* **Nucleotide-binding oligomerization domain protein 2 deficiency enhances CHOP expression and plaque necrosis in advanced atherosclerotic lesions**. The FEBS journal 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32167239
ABSTRACT
Endoplasmic reticulum (ER) stress-induced cell death of vascular smooth muscle cells (VSMCs) is extensively involved in atherosclerotic plaque stabilization. We previously reported that nucleotide-binding oligomerization domain protein 2 (NOD2) participated in vascular homeostasis and tissue injury. However, the role and underlying mechanisms of NOD2 remain unknown in ER stress-induced cell death of VSMC during vascular diseases, including advanced atherosclerosis. Here, we report that NOD2 specifically interacted with ER stress sensor activating transcription factor 6 (ATF6) and suppressed the expression of proapoptotic transcription factor CHOP (C/EBP homologous protein) during ER stress. CHOP-positive cells were increased in neointimal lesions after femoral artery injury in NOD2-deficient mice. In particular, a NOD2 ligand, MDP, and overexpression of NOD2 decreased CHOP expression in wild-type VSMCs. NOD2 interacted with an ER stress sensor molecule, ATF6, and acted as a negative regulator for ATF6 activation and its downstream target molecule, CHOP, that regulates ER stress-induced apoptosis. Moreover, NOD2 deficiency promoted disruption of advanced atherosclerotic lesions and CHOP expression in NOD2(-/-) ApoE(-/-) mice. Our findings indicate an unsuspected critical role for NOD2 in ER stress-induced cell death.

[25] *Wang S, Ran Y, Chen X et al.* **Pleiotropic Effects of Simvastatin on the Regulation of Potassium Channels in Monocytes**. Frontiers in pharmacology 2020; 11:101.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32153409

ABSTRACT

Purpose: The underlying mechanism of pleiotropic effects of statins on atherosclerosis is still unclear. Kv1.3 and KCa3.1 are two potassium channels that might be involved in monocyte migration and atherosclerosis formation. The aim of this study was to investigate the effect of simvastatin on the Kv1.3 and KCa3.1 in monocyte. Methods and Results: In human monocytic THP-1 cells, simvastatin significantly inhibited Kv1.3 mRNA and protein expression by real-time quantitative PCR analysis and western blotting. However, simvastatin had no effects on KCa3.1 mRNA and protein expression. By whole-cell patch clamp, simvastatin (10 muM) remarkably inhibited the current intensity of Kv1.3, but had no effect on KCa3.1. Simvastatin (10 muM) treatment significantly reduced the monocyte chemoattractant protein 1 (MCP-1)-induced monocyte migration. This inhibition was only partially reversed by mevalonate (1mM). In human peripheral blood mononuclear cells (PBMCs), both Kv1.3 and KCa3.1 mRNA expression were increased in patients with coronary artery diseases (CAD) (n = 20) compared to healthy controls (n = 22). However, simvastatin (40 mg per day) significantly inhibited the Kv1.3 but not KCa3.1 mRNA expression after 1 month and 3 months therapy in CAD patients. Conclusion: Our data suggested Kv1.3 in monocytes was a potential molecular target of the pleiotropic effects of statins. KCa3.1 might be another marker of CAD, but not associated with statins treatment.

[26] *Gronewold J, Kropp R, Lehmann N et al.* **Association of social relationships with incident cardiovascular events and all-cause mortality**. Heart 2020.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32165451

ABSTRACT

OBJECTIVE: To examine how different aspects of social relationships are associated with incident cardiovascular events and all-cause mortality. METHODS: In 4139 participants from the population-based Heinz Nixdorf Recall study without previous cardiovascular disease (mean (SD) age 59.1 (7.7) years, 46.7% men), the association of self-reported instrumental, emotional and financial support and social integration at baseline with incident fatal and non-fatal cardiovascular events and all-cause mortality during 13.4-year follow-up was assessed in five different multivariable Cox proportional hazards regression models: minimally adjusted model (adjusting for age, sex, social integration or social support, respectively); biological model (minimally adjusted+systolic blood pressure, low-density and high-density lipoprotein cholesterol, glycated haemoglobin, body mass index, antihypertensive medication, lipid-lowering medication and antidiabetic medication); health behaviour model (minimally adjusted+alcohol consumption, smoking and physical activity); socioeconomic model (minimally adjusted+income, education and employment); and depression model (minimally adjusted+depression, antidepressants and anxiolytics). RESULTS: 339 cardiovascular events and 530 deaths occurred during follow-up. Lack of financial support was associated with an increased cardiovascular event risk (minimally adjusted HR=1.30(95% CI 1.01 to 1.67)). Lack of social integration (social isolation) was associated with increased mortality (minimally adjusted HR=1.47 (95% CI 1.09 to 1.97)). Effect estimates did not decrease to a relevant extent in any regression model. CONCLUSIONS: Perceiving a lack of financial support is associated with a higher cardiovascular event incidence, and being socially isolated is associated with increased all-cause mortality. Future studies should investigate how persons with deficient social relationships could benefit from targeted interventions.

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[27] *Gutmann C, Siow R, Gwozdz AM et al.* **Reactive Oxygen Species in Venous Thrombosis**. International journal of molecular sciences 2020; 21.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32168908
ABSTRACT
Reactive oxygen species (ROS) have physiological roles as second messengers, but can also exert detrimental modifications on DNA, proteins and lipids if resulting from enhanced generation or reduced antioxidant defense (oxidative stress). Venous thrombus (DVT) formation and resolution are influenced by ROS through modulation of the coagulation, fibrinolysis, proteolysis and the complement system, as well as the regulation of effector cells such as platelets, endothelial cells, erythrocytes, neutrophils, mast cells, monocytes and fibroblasts. Many conditions that carry an elevated risk of venous thrombosis, such as the Antiphospholipid Syndrome, have alterations in their redox homeostasis. Dietary and pharmacological antioxidants can modulate several important processes involved in DVT formation, but their overall effect is unknown and there are no recommendations regarding their use. The development of novel antioxidant treatments that aim to abrogate the formation of DVT or promote its resolution will depend on the identification of targets that enable ROS modulation confined to their site of interest in order to prevent off-target effects on physiological redox mechanisms. Subgroups of patients with increased systemic oxidative stress might benefit from unspecific antioxidant treatment, but more clinical studies are needed to bring clarity to this issue.

[28] *Jang H, Kwak SY, Park S et al.* **Pravastatin Alleviates Radiation Proctitis by Regulating Thrombomodulin in Irradiated Endothelial Cells**. International journal of molecular sciences 2020; 21.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32164317
ABSTRACT
Although radiotherapy plays a crucial in the management of pelvic tumors, its toxicity on surrounding healthy tissues such as the small intestine, colon, and rectum is one of the major limitations associated with its use. In particular, proctitis is a major clinical complication of pelvic radiotherapy. Recent evidence suggests that endothelial injury significantly affects the initiation of radiation-induced inflammation. The damaged endothelial cells accelerate immune cell recruitment by activating the expression of endothelial adhesive molecules, which participate in the development of tissue damage. Pravastatin, a cholesterol lowering drug, exerts persistent anti-inflammatory and anti-thrombotic effects on irradiated endothelial cells and inhibits the interaction of leukocytes and damaged endothelial cells. Here, we aimed to investigate the effects of pravastatin on radiation-induced endothelial damage in human umbilical vein endothelial cell and a murine proctitis model. Pravastatin attenuated epithelial damage and inflammatory response in irradiated colorectal lesions. In particular, pravastatin improved radiation-induced endothelial damage by regulating thrombomodulin (TM) expression. In addition, exogenous TM inhibited leukocyte adhesion to the irradiated endothelial cells. Thus, pravastatin can inhibit endothelial damage by inducing TM, thereby alleviating radiation proctitis. Therefore, we suggest that pharmacological modulation of endothelial TM may limit intestinal inflammation after irradiation.

[29] *Poznyak A, Grechko AV, Poggio P et al.* **The Diabetes Mellitus-Atherosclerosis Connection: The Role of Lipid and Glucose Metabolism and Chronic Inflammation**. International journal of molecular sciences 2020; 21.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32155866

ABSTRACT
Diabetes mellitus comprises a group of carbohydrate metabolism disorders that share a common main feature of chronic hyperglycemia that results from defects of insulin secretion, insulin action, or both. Insulin is an important anabolic hormone, and its deficiency leads to various metabolic abnormalities in proteins, lipids, and carbohydrates. Atherosclerosis develops as a result of a multistep process ultimately leading to cardiovascular disease associated with high morbidity and mortality. Alteration of lipid metabolism is a risk factor and characteristic feature of atherosclerosis. Possible links between the two chronic disorders depending on altered metabolic pathways have been investigated in numerous studies. It was shown that both types of diabetes mellitus can actually induce atherosclerosis development or further accelerate its progression. Elevated glucose level, dyslipidemia, and other metabolic alterations that accompany the disease development are tightly involved in the pathogenesis of atherosclerosis at almost every step of the atherogenic process. Chronic inflammation is currently considered as one of the key factors in atherosclerosis development and is present starting from the earliest stages of the pathology initiation. It may also be regarded as one of the possible links between atherosclerosis and diabetes mellitus. However, the data available so far do not allow for developing effective anti-inflammatory therapeutic strategies that would stop atherosclerotic lesion progression or induce lesion reduction. In this review, we summarize the main aspects of diabetes mellitus that possibly affect the atherogenic process and its relationship with chronic inflammation. We also discuss the established pathophysiological features that link atherosclerosis and diabetes mellitus, such as oxidative stress, altered protein kinase signaling, and the role of certain miRNA and epigenetic modifications.

[30] *Cui J, Kessinger CW, Jhajj HS et al.* **Atorvastatin Reduces In Vivo Fibrin Deposition and Macrophage Accumulation, and Improves Primary Patency Duration and Maturation of Murine Arteriovenous Fistula**. Journal of the American Society of Nephrology : JASN 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32152232

ABSTRACT
BACKGROUND: Arteriovenous fistulas placed surgically for dialysis vascular access have a high primary failure rate resulting from excessive inward remodeling, medial fibrosis, and thrombosis. No clinically established pharmacologic or perisurgical therapies currently address this unmet need. Statins' induction of multiple anti-inflammatory and antithrombotic effects suggests that these drugs might reduce arteriovenous fistula failure. Yet, the in vivo physiologic and molecular effects of statins on fistula patency and maturation remain poorly understood. METHODS: We randomized 108 C57Bl/6J mice to receive daily atorvastatin 1.14 mg/kg or PBS (control) starting 7 days before end-to-side carotid artery-jugular vein fistula creation and for up to 42 days after fistula creation. We then assessed longitudinally the effects of statin therapy on primary murine fistula patency and maturation. We concomitantly analyzed the in vivo arteriovenous fistula thrombogenic and inflammatory macrophage response to statin therapy, using the fibrin-targeted, near-infrared fluorescence molecular imaging agent FTP11-CyAm7 and dextranated, macrophage-avid nanoparticles CLIO-VT680. RESULTS: In vivo molecular-structural imaging demonstrated that atorvastatin significantly reduced fibrin deposition at day 7 and macrophage accumulation at days 7 and 14, findings supported by histopathologic and gene-expression analyses. Structurally, atorvastatin promoted favorable venous limb outward remodeling, preserved arteriovenous fistula blood flow, and prolonged primary arteriovenous fistula patency through day 42 ($P<0.05$ versus control for all measures). CONCLUSIONS: These findings provide new in

vivo evidence that statins improve experimental arteriovenous fistula patency and maturation, indicating that additional clinical evaluation of statin therapy in patients on dialysis undergoing arteriovenous fistula placement is warranted.

[31] *Zheng J, Brion MJ, Kemp JP et al.* **The Effect of Plasma Lipids and Lipid-Lowering Interventions on Bone Mineral Density: A Mendelian Randomization Study**. J Bone Miner Res 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32163637
ABSTRACT
Several epidemiological studies have reported a relationship between statin treatment and increased bone mineral density (BMD) and reduced fracture risk, but the mechanism underlying the purported relationship is unclear. We used Mendelian randomization (MR) to assess whether this relationship is explained by a specific effect in response to statin use or by a general effect of lipid lowering. We utilized 400 single-nucleotide polymorphisms (SNPs) robustly associated with plasma lipid levels as exposure. The outcome results were obtained from a heel estimated BMD (eBMD) genomewide association study (GWAS) from the UK Biobank and dual-energy X-ray absorptiometry (DXA) BMD at four body sites and fracture GWAS from the GEFOS consortium. We performed univariate and multivariable MR analyses of low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride levels on BMD and fracture. Univariate MR analyses suggested a causal effect of LDL-C on eBMD (beta = -0.06; standard deviation change in eBMD per standard deviation change in LDL-C, 95% confidence interval [CI] = -0.08 to -0.04; p = 4 x 10(-6)), total body BMD (beta = -0.05, 95% CI = -0.08 to -0.01, p = 6 x 10(-3)) and potentially on lumbar spine BMD. Multivariable MR suggested that the effects of LDL-C on eBMD and total body BMD were independent of HDL-C and triglycerides. Sensitivity MR analyses suggested that the LDL-C results were robust to pleiotropy. MR analyses of LDL-C restricted to SNPs in the HMGCR region showed similar effects on eBMD (beta = -0.083; -0.132 to -0.034; p = 0.001) to those excluding these SNPs (beta = -0.063; -0.090 to -0.036; p = 8 x 10(-6)). Bidirectional MR analyses provided some evidence for a causal effect of eBMD on plasma LDL-C levels. Our results suggest that effects of statins on eBMD and total body BMD are at least partly due to their LDL-C lowering effect. Further studies are required to examine the potential role of modifying plasma lipid levels in treating osteoporosis. (c) 2020 American Society for Bone and Mineral Research.

[32] *Ramhormozi P, Mohajer Ansari J, Simorgh S, Nobakht M*. **Bone-Marrow-Derived Mesenchymal Stem Cells (BMSCs) combined with Simvastatin accelerates burn wound healing by activation of the Akt/mTOR pathway**. J Burn Care Res 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32157277
ABSTRACT
Burn wound healing is one of the most important problems in the field of medical science. Promising results have recently been reported by researchers who used bone marrow mesenchymal stem cells (BMSCs) to treat burn wounds. In this study, we investigated the effects of BMSC therapy in combination with simvastatin (SMV) on angiogenesis as well as on the activity of the Akt/mTOR signaling pathway during burn wound healing in rats. After creating second-degree burn wounds, 40 adult male Wistar rats were randomly divided into four treatment groups: the control, SMV, BMSCs, and the combination therapy group (BMSCs+SMV). Animals were sacrificed 14 days after treatment initiation and the wounds were removed for histological and molecular analyses. All in all, combination

therapy produced better outcomes than individual therapy in terms of the wound closure area, epidermal regeneration level, collagen deposition intensity, and re-epithelialization rate. In addition, the elevations of expression levels of Akt and mTOR genes, at both mRNA and protein levels, were more pronounced in the BMSCs+SMV group (P<0.05, at least, for both qRT-PCR and western blot assessments). qRT-PCR findings also demonstrated that the wounds treated with the combination of BMSCs and Smv had the highest expression levels of CD31 and VEGF genes (P<0.01 for all comparisons). These data suggest that the combined administration of BMSCs transplantation and topical SMV has a great potential in burn wound healing. According to the findings, the beneficial effects of the combination therapy are caused, at least in part, through stimulating Akt/mTOR signaling pathway.

[33] *Galiano M, Hammersen J, Sauerstein K et al.* **Homozygous familial hypercholesterolemia with severe involvement of the aortic valve-A sibling-controlled case study on the efficacy of lipoprotein apheresis**. Journal of clinical apheresis 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32163632
ABSTRACT
BACKGROUND: Homozygous familial hypercholesterolemia (hoFH) can cause severe atherosclerotic cardiovascular disease (ASCVD) in early infancy. Diagnosis and initiation of effective lipid-lowering therapy (LLT) are recommended as early as possible to prevent ASCVD-related morbidity and mortality. METHODS: The clinical courses of a pair of siblings with an identical hoFH genotype, who exhibited major similarities of their clinical phenotype were analyzed in a case-control fashion including the family. RESULTS: The older sibling was diagnosed with hoFH at the age of 4. Untreated LDL-cholesterol (LDL-C) was 17 mmol/L (660 mg/dL). LLT including lipoprotein apheresis (LA) was initiated and has been successful for 8 years now. A reduction of estimated cholesterol burden by 74% was achieved by LA and combined drug therapy including statins and ezetimibe. The efficacy of escalation of drug therapy was limited because the underlying LDL receptor (LDLR) mutation in the family resulted in substantially reduced receptor function. Treatment with proprotein convertase subtilisin-kexin type 9 (PCSK9)-antibodies failed. His younger brother died at the age of 2 years shortly after the hoFH diagnosis of the elder sibling. Postmortem examination revealed advanced aortic root atheroma and aortic valve stenosis. In the older sibling, aortic valve stenosis and insufficiency were treated at the age of 9 years with mechanical aortic valve replacement. CONCLUSIONS: LLT including LA should be initiated as early as possible following the diagnosis of hoFH with very high LDL-C levels. With the same genotype, the phenotype of hoFH can exhibit similar patterns but outcome is substantially related to treatment.

[34] *Xue J, Wu Z, Gong S et al.* **High-dose atorvastatin improves vascular endothelial function in patients with leukoaraiosis**. Journal of clinical laboratory analysis 2020; 34:e23081.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32154613
ABSTRACT
OBJECTIVE: Leukoaraiosis (LA), as an age-related white matter degeneration, is mainly caused by chronic ischemia. Our study aims to explore the efficacy of different doses of atorvastatin (ATV) in the vascular endothelial function in patients with LA. METHODS: Our study enrolled 402 LA patients who were then randomly included as control or treated with ATV (10 mg), ATV (20 mg), or ATV (30 mg). The total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were detected by enzyme colorimetric assay. The high-sensitivity C-

reactive protein (hs-CRP) level, reactive hyperemia index (RHI), endothelin-1 (ET-1) content, and nitric oxide (NO) level were tested by latex agglutination test, peripheral arterial tonometry technology, radioimmunoassay, and nitrate reductase assay, respectively. RESULTS: After 8 weeks of ATV treatment, the levels of TC, LDL-C, and HS-CRP decreased significantly, and the trends were demonstrated in a more significant way with the increases of dose of ATV. The treatment with ATV at different doses elevated NO level and RHI and declined ET-1 content. Gastrointestinal reaction, muscular pain, and increased aminopherase were observed after treatment with the ATV at different doses with more obvious symptoms detected accompanied by the increase of the dose. The RHI was in negative correlation with the ET-1 and HS-CRP while in positive correlation with NO. CONCLUSION: Our study demonstrates that ATV can significantly improve the vascular endothelial function in LA patients with a dose-dependent effect.

[35] *van den Beukel TC, Lucci C, Hendrikse J et al.* **Risk factors for calcification of the vertebrobasilar arteries in cardiovascular patients referred for a head CT, the SMART study**. Journal of neuroradiology. Journal de neuroradiologie 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32169469
ABSTRACT
BACKGROUND AND PURPOSE: Vertebrobasilar artery calcification (VBAC) has been associated with increased stroke occurrence. Little is known on VBAC risk factors, especially for patients with cardiovascular disease. We aimed to assess risk factors associated with VBAC in a cohort of cardiovascular patients referred for a head computed tomography (CT) scan. MATERIALS AND METHODS: All patients who underwent a clinically indicated, unenhanced, thin slice head CT 6 months before or after inclusion in the SMART study were included. CTs were assessed for presence of VBAC (dichotomously). Relative risks of the associations of age, sex, diabetes mellitus (DM), obesity, body mass index, estimated glomerular filtration rate, hypertension, hyperlipidemia, use of lipid lowering medication, smoking status, high sensitivity C-reactive protein, ankle-brachial index (ABI; </=0.90, >/=1.30, continuous), internal carotid artery stenosis >/=70%, and carotid intima-media thickness (IMT) with VBAC were estimated using Poisson regression analysis with robust standard errors, adjusted for age and sex. RESULTS: Of the 471 patients included (57% male, median age 58 [interquartile range 47-63]), 117 (24.8%) showed VBAC. Presence of VBAC was associated with older age (RR per 10 years=1.70 [95%CI 1.46-1.99]), DM (RR=1.45 [95%CI 1.03-2.06]), obesity (RR=1.53 [95%CI 1.10-2.12]), ABI </=0.90 (RR=1.57 [95%CI 1.02-2.41]), and an increased carotid IMT (RR=2.60 per mm [95%CI 1.20-5.62]). Other measurements were not associated with VBAC. CONCLUSIONS: We identified several markers associated with VBAC in patients with cardiovascular disease referred for a head CT. Future investigation into the relationship between VBAC and stroke is warranted to determine the potential of VBAC in stroke prevention.

[36] *Zheng PF, Liao FJ, Yin RX et al.* **Genes associated with inflammation may serve as biomarkers for the diagnosis of coronary artery disease and ischaemic stroke**. Lipids in health and disease 2020; 19:37.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32164735
ABSTRACT
BACKGROUND: The current research aimed to expound the genes and pathways that are involved in coronary artery disease (CAD) and ischaemic stroke (IS) and the related mechanisms. METHODS: Two

array CAD datasets of (GSE66360 and GSE97320) and an array IS dataset (GSE22255) were downloaded. Differentially expressed genes (DEGs) were identified using the limma package. The online tool Database for Annotation, Visualization and Integrated Discovery (DAVID) (version 6.8; david.abcc.ncifcrf.gov) was used to annotate the Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway and Gene Ontology (GO) enrichment analyses of the DEGs. A protein-protein interaction (PPI) network was constructed by Cytoscape software, and then Molecular Complex Detection (MCODE) analysis was used to screen for hub genes. The hub genes were also confirmed by RT-qPCR and unconditional logistic regression analysis in our CAD and IS patients. RESULTS: A total of 20 common DEGs (all upregulated) were identified between the CAD/IS and control groups. Eleven molecular functions, 3 cellular components, and 49 biological processes were confirmed by GO enrichment analysis, and the 20 common upregulated DEGs were enriched in 21 KEGG pathways. A PPI network including 24 nodes and 68 edges was constructed with the STRING online tool. After MCODE analysis, the top 5 high degree genes, including Jun proto-oncogene (JUN, degree = 9), C-X-C motif chemokine ligand 8 (CXCL8, degree = 9), tumour necrosis factor (TNF, degree = 9), suppressor of cytokine signalling 3 (SOCS3, degree = 8) and TNF alpha induced protein 3 (TNFAIP3, degree = 8) were noted. RT-qPCR results demonstrated that the expression levels of CXCL8 were increased in IS patients than in normal participants and the expression levels of SOCS3, TNF and TNFAIP were higher in CAD/IS patients than in normal participants. Meanwhile, unconditional logistic regression analysis revealed that the incidence of CAD or IS was positively correlated with the CXCL8, SOCS3, TNF and TNFAIP3. CONCLUSIONS: The CXCL8, TNF, SOCS3 and TNFAIP3 associated with inflammation may serve as biomarkers for the diagnosis of CAD or IS. The possible mechanisms may involve the Toll-like receptor, TNF, NF-kappa B, cytokine-cytokine receptor interactions and the NOD-like receptor signalling pathways.

[37] *DiNicolantonio JJ, O'Keefe JH*. **The Benefits of Omega-3 Fats for Stabilizing and Remodeling Atherosclerosis**. Missouri medicine 2020; 117:65-69.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32158053
ABSTRACT
The majority of acute coronary syndromes are caused by the rupture of plaques rendered vulnerable by oxidized lipids, inflammation, and a thin fibrous cap with reduced collagen and smooth muscle cell content.2 Thus, stabilizing and reversing vulnerable atherosclerotic plaques can help to prevent cardiovascular events. In this regard, long-chain omega-3 fatty acids have a plethora of data for stabilizing vulnerable atherosclerotic plaques as well as reversing atherosclerosis. This review paper will summarize the observational data as well as animal and human studies supporting such a role and further discuss the current controversies around omega-3 supplementation.

[38] *Braz NFT, Pinto MRC, Vieira ELM et al.* **Renin-angiotensin system molecules are associated with subclinical atherosclerosis and disease activity in rheumatoid arthritis**. Modern rheumatology 2020:1-8.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32149558
ABSTRACT
Objectives: To compare serum levels of RAS components in women with RA versus healthy females and to investigate the association between these molecules and subclinical atherosclerosis.Methods: A cross-sectional study involving female RA patients without ischemic CVD. Disease activity was assessed using the DAS28 and the CDAI. IMT of the common carotid artery was evaluated by ultrasonography.

Serum levels of Ang II, Ang-(1-7), ACE and ACE2 were determined by enzyme immunoassay.Results: Fifty women with RA, mean 48.2 (7.3) years, were compared to 30 healthy women, paired by age. RA patients had higher plasma levels of Ang II ($p < .01$), Ang-(1-7) ($p < .01$), and ACE ($p < .01$) than controls. The ratios of ACE to ACE2 were higher in RA patients, whereas Ang II/Ang-(1-7) ratios were lower in RA patients. The presence of hypertension and the treatment with ACE inhibitors did not significantly modify serum levels of Ang II, Ang-(1-7), ACE and ACE2 in patients with RA. Seven RA patients had altered IMT, and eight patients exhibited atherosclerotic plaque. There was a negative correlation between ACE2 levels and IMT ($p = .041$). IMT positively correlated with age ($p = .022$), disease duration ($p = .012$) and overall Framingham risk score ($p = .008$). Ang II concentrations positively correlated with DAS28 ($p = .034$) and CDAI ($p = .040$).Conclusion: Patients with RA had an activation of the RAS, suggesting an association with disease activity and cardiovascular risk.Rheumatological key messagesImbalance of both RAS axes may be associated with cardiovascular risk and disease activity in rheumatoid arthritis.Ultrasonography of the carotid arteries can identify early, subclinical atherosclerotic disease in rheumatoid arthritis patients.Angiotensin-converting enzyme inhibition or angiotensin 1 receptor blockade may be beneficial for rheumatoid arthritis patients.

[39] *Kerr AJ, Mitnala S, Lee M, White HD*. **Utilisation and maintenance of high-intensity statins following acute coronary syndrome and coronary angiography: opportunities to improve care (ANZACS-QI 26)**. The New Zealand medical journal 2020; 133:21-40.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32161419

ABSTRACT

AIMS: A key pillar in the medical management of patients after an acute coronary syndrome (ACS) is the early initiation and maintenance of "high-intensity" statin therapy to lower low-density lipoprotein cholesterol (LDL-C) and to improve clinical outcomes. The aim of this study was to describe the New Zealand utilisation of high-intensity statin therapy in the first year post-ACS. METHODS: 19,867 New Zealand patients (>/=20 years), discharged post-ACS event (2015-2017) were identified from the All New Zealand ACS Quality Improvement (ANZACS-QI) registry and anonymously linked with the national pharmaceutical dataset to identify statin dispensing early (0-3 months) and late (9-12 months) post-discharge. "High intensity" statin was subdivided into the New Zealand guidelines recommended dose (80mg atorvastatin) and "other high-intensity" statin (atorvastatin 40mg, simvastatin 80mg). All other statin doses were classified as "low/medium dose". RESULTS: Seventy-nine percent were initially dispensed high-intensity statins. Thirty-six percent of the overall cohort received 80mg atorvastatin and 43% a lower "other high-intensity" statin. A further 13% received a medium/low dose and 8% no statin. By 12 months, 29% were dispensed atorvastatin 80mg, 36% another high dose, 14% a low/medium dose and 21% no statin. Only 14% of those initially on 80mg atorvastatin had a statin dose reduction. After multivariable adjustment, the risk of discontinuation was the same for those started on atorvastatin 80mg compared with "other high dose", and lower than for those started on a low/medium dose. Few patients (6.2%) had statins started, or dose up-titrated post-discharge. There is clinically unexplained variation in the use of the highest atorvastatin 80mg dose between district health boards (range 15% to 65%). CONCLUSIONS: Eight in 10 ACS patients were dispensed a high-intensity statin at discharge, but only 36% received the guidelines-recommended dose of 80mg of atorvastatin. By one year, one in five patients discharged on a statin were not receiving it. There are opportunities to improve longer-term LDL-C reduction and clinical outcomes through dosage optimisation and improved medication maintenance.

[40] *Drehmer E, Platero JL, Carrera-Julia S et al.* **The Relation between Eating Habits and Abdominal Fat, Anthropometry, PON1 and IL-6 Levels in Patients with Multiple Sclerosis**. Nutrients 2020; 12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32168955

ABSTRACT

BACKGROUND: Multiple sclerosis (MS) is a chronic neurodegenerative disease of an inflammatory, demyelinating and autoimmune nature. Diets with a high caloric density could be especially relevant in terms of the pathogenesis related to an increase in adipose tissue that is metabolically active and releases mediators, which can induce systemic inflammation and an increased oxidation state. The aim of this study was to analyse the eating habits related to calorie intake and their impact on abdominal obesity associated with anthropometric variables, the activity of the oxidation marker paraoxonase 1 (PON1), and interleukin 6 (IL-6) levelsin MS patients. METHODS: An analytical and quantitative observational study was conducted with a population of 57 MS patients. The dietary-nutritional anamnesis was gained through the Food Frequency Questionnaire and a food diary. Diet and eating habits have been analysed through the Easy Diet-Programa de gestion de la consulta(R) software. Anthropometric measurements were taken in order to determine the presence of abdominal obesity. In addition, PON1 was quantified in serum by means of automated spectrophotometric assays and IL-6 was quantified using the ELISA technique. RESULTS: A normal calorie intake was determined for women, yet a slightly lower intake was observed in men. Carbohydrate consumption was below what was established, and protein and lipids were over, in both cases. Furthermore, most patients had abdominal obesity, with significantly higher body mass index (BMI), waist-to-hip ratio (WHR), waist-to-height ratio (WHtR), fat percentage and IL-6 levels. IL-6 is greatly correlated with waist circumference and WHtR. CONCLUSION: MS patients' nutrient intake shows an imbalance between macronutrients. This seems to favour the abdominal obesity associated with high values of proinflammatory IL-6 that is not correlated with a lower activity of PON1.

[41] *Seamon K, Sanfilippo F, Bulsara M et al.* **Predictors of ceasing or reducing statin medication following a large increase in the consumer copayment for medications: a retrospective observational study**. Public health research & practice 2020; 30.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32152615

ABSTRACT

OBJECTIVES: Previous Australian research has shown that following the 21% increase in patient copayments for medications on the Pharmaceutical Benefits Scheme (PBS) in 2005, the use of lipid-lowering therapy declined by 5%. This study aimed to determine the demographic and clinical characteristics of individuals who continued, reduced or ceased their use of statin medication in 2005. STUDY TYPE: Retrospective observational study using routinely collected administrative data. METHOD: We used pharmaceutical claims, hospital separations and mortality records from 2000 to 2005 for the Western Australian population. The cohort comprised stable users of statin medication in 2004. Based on changes in statin use between 2004 and 2005, we identified individuals who: 1) continued using statins; 2) reduced their use by >/=20%; or 3) ceased therapy for at least the first 6 months in 2005. Multivariate logistic regression models were used to determine whether the demographic and clinical characteristics of the three groups differed. RESULTS: There were 205 924 statin users identified in Western Australia as of December 2004. After the January 2005 Pharmaceutical Benefits Scheme (PBS) copayment increase, 3.2% of users ceased their regular statin

therapy, 12.9% reduced statin use and 83.9% continued statin use. This represented a 2.1% increase in statin users reducing or ceasing therapy compared to 2004. Predictors of cessation and reduction of statin therapy included younger age, greater socio-economic disadvantage, residing in very remote areas, having general beneficiary status, being a new statin user, having no prior history of ischaemic heart disease, having no prior history of a coronary artery revascularisation procedure, taking no other cardiovascular medication or diabetic medication, taking an increased number of medications, and having a lower level of adherence to statin medication in 2004. CONCLUSION: Compared to 2004, an additional 2.1% of statin users reduced or discontinued medication use in 2005, which may be attributed to an increase in the medication copayment. Individuals with general beneficiary status, and younger and healthier people were at particular risk of cessation or reduction in statin use in 2005.

[42] *McWilliam SJ, Rosala-Hallas A, Jones AP et al.* **Author Correction: A randomised controlled trial of rosuvastatin for the prevention of aminoglycoside-induced kidney toxicity in children with cystic fibrosis**. Scientific reports 2020; 10:4730.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32152372
ABSTRACT
An amendment to this paper has been published and can be accessed via a link at the top of the paper.

[43] *Williams PT*. **Gene-environment interactions due to quantile-specific heritability of triglyceride and VLDL concentrations**. Scientific reports 2020; 10:4486.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32161301
ABSTRACT
"Quantile-dependent expressivity" is a dependence of genetic effects on whether the phenotype (e.g., triglycerides) is high or low relative to its distribution in the population. Quantile-specific offspring-parent regression slopes (betaOP) were estimated by quantile regression for 6227 offspring-parent pairs. Quantile-specific heritability (h(2)), estimated by 2betaOP/(1 + rspouse), decreased 0.0047 +/- 0.0007 (P = 2.9 x 10(-14)) for each one-percent decrement in fasting triglyceride concentrations, i.e., h(2) +/- SE were: 0.428 +/- 0.059, 0.230 +/- 0.030, 0.111 +/- 0.015, 0.050 +/- 0.016, and 0.033 +/- 0.010 at the 90th, 75th, 50th, 25th, and 10th percentiles of the triglyceride distribution, respectively. Consistent with quantile-dependent expressivity, 11 drug studies report smaller genotype differences at lower (post-treatment) than higher (pre-treatment) triglyceride concentrations. This meant genotype-specific triglyceride changes could not move in parallel when triglycerides were decreased pharmacologically, so that subtracting pre-treatment from post-treatment triglyceride levels necessarily created a greater triglyceride decrease for the genotype with a higher pre-treatment value (purported precision-medicine genetic markers). In addition, sixty-five purported gene-environment interactions were found to be potentially attributable to triglyceride's quantile-dependent expressivity, including gene-adiposity (APOA5, APOB, APOE, GCKR, IRS-1, LPL, MTHFR, PCSK9, PNPLA3, PPARgamma2), gene-exercise (APOA1, APOA2, LPL), gene-diet (APOA5, APOE, INSIG2, LPL, MYB, NXPH1, PER2, TNFA), gene-alcohol (ALDH2, APOA5, APOC3, CETP, LPL), gene-smoking (APOC3, CYBA, LPL, USF1), gene-pregnancy (LPL), and gene-insulin resistance interactions (APOE, LPL).

[44] *Kizilirmak P, Ongen Z, Kayikcioglu M, Tokgozoglu L*. **[Evaluation of statin use on LDL cholesterol levels in Turkey: A systematic review]**. Turk Kardiyoloji Dernegi arsivi : Turk Kardiyoloji Derneginin yayin organidir 2020; 48:137-148.

Literature update week 11 (2020)

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32147651

ABSTRACT

OBJECTIVE: The aim of this study was to examine and present the effect of statin treatment on the low-density lipoprotein (LDL) cholesterol level of patients in Turkey by evaluating the data of studies conducted in the country. METHODS: Manuscripts published between January 1, 2008 and December 31, 2017 with terms 'LDL' and 'TURK' in the title or abstract and reporting LDL cholesterol data of patients treated with statins were evaluated for inclusion in the study. From the initial search result a total of 1795 papers, 39 manuscripts with 63 study arms were selected for analysis and the data of 3486 patients were included. Descriptive analysis was used to assess the data. Weighted averages of the data were also calculated. RESULTS: The female/male ratio was 42/58. The mean age was 52.9+/-10.1 years. The proportion of patients with the recommended LDL cholesterol level of <70 mg/dL after treatment with statins was 15.3%;. In all, 10.2% of the patients who were prescribed a low-dose statin and 28.0% of those who were prescribed a high-dose statin had an LDL cholesterol of <70 mg/dL after treatment. Among patients who were being treated with statins for </=2 months, 25.7% achieved an LDL cholesterol level of <70 mg/dL. Among those who were being treated with statins for 2-4 months and >4 months the proportion was 11.4% and 9.7%, respectively. The percentage of patients at the target level was 21.8%, 21.7%, 17.9%;, 8.6%, and 0.8% among those using atorvastatin, simvastatin, rosuvastatin, fluvastatin, and pravastatin, respectively. CONCLUSION: In Turkey, only 15% of the patients who had received statin therapy had a LDL cholesterol level of <70 mg/dL. Revision of the current treatment should be considered to reach the target levels recommended in the guidelines, especially for patients with high cardiovascular risk.