Literature update week 46 (2018)

[1] *Marazzi G, Campolongo G, Pelliccia F et al.* **Usefulness of Low-Dose Statin Plus Ezetimibe and/or Nutraceuticals in Patients With Coronary Artery Disease Intolerant to High-Dose Statin Treatment**. The American journal of cardiology 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30420184
ABSTRACT
High-dose statin (HDS) therapy is recommended to reduce low-density lipoprotein cholesterol (LDL-C); however, some patients are unable to tolerate the associated side effects. Nutraceuticals have shown efficacy in lowering LDL-C. The aim of this study was to evaluate whether the combination of low-dose statin (LDS) plus ezetimibe (EZE) or LDS plus nutraceutical (Armolipid Plus [ALP] containing red yeast rice, policosanol, and berberine) can lead to a higher proportion of high-risk patients achieving target LDL-C. A secondary objective was to assess the efficacy of triple combination LDS+EZE+ALP in resistant patients (LDL-C >70 mg/dl). A randomized, prospective, parallel-group, single-blind study was conducted in patients with coronary artery disease (n = 100) who had undergone percutaneous coronary intervention in the preceding 12 months, were HDS-intolerant, and were not at LDL-C target (<70 mg/dl) with LDS alone. Patients received either LDS+EZE or LDS+ALP. Of the 100 patients, 33 patients (66%) treated with LDS+EZE and 31 patients (62%) treated with LDS+ALP achieved target LDL-C after 3 months, which was maintained at 6 months. Patients who did not achieve the therapeutic goal received a triple combination of LDS+EZE+ALP for a further 3 months. At 6 months, 28 of 36 patients (78%) achieved LDL-C target. Overall, 92% of patients enrolled in this study were at target LDL-C at 6 months. No patients in any group experienced major side effects. In conclusion, in HDS-intolerant coronary artery disease patients, the combination of LDS plus EZE and/or ALP represents a valuable therapeutic option allowing most patients to reach target LDL-C within 3 to 6 months.

[2] *Clemente-Postigo M, Oliva-Olivera W, Coin-Araguez L et al.* **METABOLIC ENDOTOXEMIA PROMOTES ADIPOSE DYSFUNCTION AND INFLAMMATION IN HUMAN OBESITY**. American journal of physiology. Endocrinology and metabolism 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30422702
ABSTRACT
Impaired adipose tissue (AT) lipid handling and inflammation is associated with obesity-related metabolic diseases. Circulating lipopolysaccharides (LPS) from gut microbiota (metabolic endotoxemia), proposed as a triggering factor for the low-grade inflammation in obesity, might also be the responsible for AT dysfunction. Nevertheless, this hypothesis has not been explored in human obesity. In order to analyze the relationship between metabolic endotoxemia and AT markers for lipogenesis, lipid handling and inflammation in human obesity, 33 obese patients scheduled for surgery were recruited and classified according to their LPS levels. Visceral and subcutaneous AT gene and protein expression were analyzed and adipocyte and AT in vitro assays performed. Obese subjects with a high degree of metabolic endotoxemia had lower expression of key genes for AT function and lipogenesis (SREBP1, FABP4, FASN and LEP), but higher expression of inflammatory genes in visceral and subcutaneous AT than subjects with low LPS levels. In vitro experiments corroborated that LPS are responsible for the adipocyte and AT inflammation and down-regulation of PPARG, SCD, FABP4 and LEP expression and LEP secretion. Thus, metabolic endotoxemia influences AT physiology in human obesity by

decreasing the expression of factors involved in AT lipid handling and function as well as by increasing inflammation.

[3] *Beharry KD, Cai CL, Siddiqui F et al.* **Comparative Effects of Coenzyme Q10 or n-3 Polyunsaturated Fatty Acid Supplementation on Retinal Angiogenesis in a Rat Model of Oxygen-Induced Retinopathy**. Antioxidants (Basel, Switzerland) 2018; 7.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30423931
ABSTRACT
Neonatal intermittent hypoxia (IH) or apnea afflicts 70% to 90% of all preterm infants <28 weeks gestation, and is associated with severe retinopathy of prematurity (ROP). We tested the hypotheses that coenzyme Q10 (CoQ10) or omega-3 polyunsaturated fatty acids (n-3 PUFAs) supplementation during neonatal IH reduces the severity of oxygen-induced retinopathy (OIR). Newborn rats were exposed to two IH paradigms: (1) 50% O(2) with brief hypoxia (12% O(2)); or (2) 21% O(2) with brief hypoxia, until postnatal day 14 (P14), during which they received daily oral CoQ10 in olive oil, n-3 PUFAs in fish oil, or olive oil only and compared to room air (RA) treated groups. Pups were examined at P14, or placed in RA until P21. Retinal angiogenesis, histopathology, and morphometry were determined. Both IH paradigms produced severe OIR, but these were worsened with 50/12% O(2) IH. CoQ10 and n-3 PUFAs reduced the severity of OIR, as well as ocular growth factors in both IH paradigms, but CoQ10 was more effective in 50/12% O(2) IH. Supplementation with either CoQ10 or n-3 PUFAs targeting IH-induced retinal injury is individually effective for ameliorating specific characteristics consistent with ROP. Given the complexity of ROP, further studies are needed to determine whether combined CoQ10 and n-3 PUFAs supplementation would optimize their efficacy and result in a better outcome.

[4] *Garcia-Mendez RC, Almeida-Gutierrez E, Serrano-Cuevas L et al.* **Reduction of No Reflow with a Loading Dose of Atorvastatin before Primary Angioplasty in Patients with Acute ST Myocardial Infarction**. Arch Med Res 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30446246
ABSTRACT
BACKGROUND: No reflow defined as an altered myocardial reperfusion and failure at microvascular level is a frequent complication in acute myocardial infarction that attenuates beneficial effect of reperfusion therapy leading to poor outcomes. There is not enough evidence to support that previous use of statins improves coronary flow in patients undergoing primary percutaneous coronary intervention (PCI). AIM OF STUDY: To determine if a loading dose of 80 mg of atorvastatin before primary angioplasty reduces the frequency of no reflow, hs-CRP, IL6 intracoronary levels, and major combined cardiovascular events at 30 d. METHODS: In this controlled clinical trial, we randomly assigned 103 adult patients within the 12 h of acute ST-elevation myocardial infarction (STEMI) to receive 80 mg of atorvastatin additional to standard treatment (AST) before performing primary PCI versus standard treatment (ST) alone. The primary outcomes were the occurrence of no reflow and high sensitivity C-reactive protein (hs-CRP) and interleukin 6 levels and secondary outcomes were major adverse cardiovascular events at 30 d. RESULTS: 103 patients were analyzed, 49 (48%) received AST, 54 (52%) ST. Frequency of no reflow among groups was 27 vs. 63% respectively, p </=0.0001. hs-CRP level

was 2.69 mg/dL for AST vs. 2.2 mg/dL in ST, meanwhile IL-6 levels were 5.2 pg/mL vs. 6.35 pg/mL respectively, p = ns. Cox regression model demonstrated that the treatment assigned is an independent predictor for no reflow occurrence (HR 0.34 95%, CI 0.18-0.61, p </=0.001). CONCLUSION: The administration of a loading dose of 80 mg atorvastatin before primary PCI is an effective strategy for prevention of no reflow improving also clinical outcomes and free survival rate for the presentation of major adverse cardiovascular events at 30 d.

[5] *Alhababi D, Zayed H*. **Spectrum of mutations of familial hypercholesterolemia in the 22 Arab countries**. Atherosclerosis 2018; 279:62-72.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30415195
ABSTRACT
BACKGROUND AND AIMS: Familial hypercholesterolemia (FH) is an inherited genetic disorder of lipid metabolism characterized by a high serum LDL-cholesterol profile and xanthoma formation, and FH increases the risk of premature atherosclerosis and cardiovascular disease (CVD). Mutations in the low-density lipoprotein (LDLR), apolipoprotein B (APOB), proprotein convertase subtilisin/kexin 9 (PCSK9), and LDLRAP1 genes have been associated with FH. Although FH is a major risk for CVD, the disease prevalence and its underlying molecular basis in the 22 Arab countries are still understudied. This study aimed to analyze all peer-reviewed studies related to the prevalence of FH and its causative mutations in the 22 Arab countries. METHODS: We searched five literature databases (Scopus, Science Direct, Web of Science, PubMed, and Google Scholar) from inception until June 2018, using all possible search terms to capture all of the genetic and prevalence data related to Arab patients with FH. RESULTS: A total of 5,484 titles and abstracts were identified; 51 studies met our inclusion criteria for the final systematic review. Fifty-one mutations in Arab patients with FH were identified in only eight Arab countries; 47 were identified in the LDLR gene, two in the PCSK9 gene, and two in LDLRAP1 gene. Twenty mutations in the LDLR gene were distinctive to Arab patients. A few studies reported prevalence estimates, ranging from 0.4% to 6.8%. CONCLUSIONS: This is the first systematic review to dissect the up-to-date status of the genetic epidemiology of Arab patients with FH. It seems that FH is underdiagnosed and that its prevalence is understudied due to the dearth of published information about Arab patients with FH. Therefore, there is a need for well-controlled genetic epidemiological studies on Arab patients with FH.

[6] *Woodman RJ, Baghdadi LR, Shanahan EM et al.* **Diets high in n-3 fatty acids are associated with lower arterial stiffness in patients with rheumatoid arthritis: a latent profile analysis**. The British journal of nutrition 2018:1-13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30430957
ABSTRACT
Supplementation with n-3 fatty acids can influence inflammation and markers of arterial stiffness that are increased in patients with rheumatoid arthritis (RA). However, it is unknown whether specific patterns of dietary fatty acid intake are similarly associated. In a longitudinal study, eighty-six RA patients reported their dietary intake and had arterial stiffness measured using the augmentation index (AIx) at baseline and 8 months. Latent profile analysis (LPA) was performed to characterise patterns of fatty acid intake using sixteen major fatty acids. Models for two to six profiles were compared using the Akaike and Bayesian information criteria.

Associations between AIx and the profiles were adjusted for age, sex, disease activity, fish oil supplementation, medications, physical activity and socio-economic status. LPA identified five distinct profiles. Profile 1 subjects (n 7) reported significantly higher intake of palmitoleic acid (16 : 1), arachidonic acid (20 : 4n-6), EPA (20 : 5n-3), DHA (22 : 6n-3) and docosapentaenoic acid (22 : 5n-3) (P<0.001 for each) than profiles 2 (n 14), 3 (n 19), 4 (n 23) and 5 (n 23) and significantly higher grilled and tinned fish consumption. The AIx varied significantly across the five profiles (P=0.023); subjects in profile 1 had a significantly lower AIx than those in profile 3 (beta=-7.2 %; 95 % CI -11.5, -2.9; P=0.001) who had the lowest reported intake of n-3 fatty acids. Fish oil supplementation was also independently associated with lower AIx (beta=-4.15 %; 95 % CI -6.73, -1.56; P=0.002). A diet characterised by a higher reported intake of n-3 fatty acids, palmitoleic acid (16 : 1) and arachidonic acid (20 : 4n-6) is associated with a lower AIx in RA patients.

[7] *Stamenkovic A, Pierce GN, Ravandi A*. **Oxidized Lipids: Not just another brick in the wall**. Canadian journal of physiology and pharmacology 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30444647
ABSTRACT
Over the past decade there has been intense investigation in trying to understand the pathological role that oxidized phospholipids play in cardiovascular disease. Phospholipids are targets for oxidation, particularly during conditions of excess free radical generation. Once oxidized, they acquire novel roles uncharacteristic of their precursors. Oxidized phosphatidylcholines have an important role in multiple physiological and pathophysiological conditions including atherosclerosis, neurodegenerative diseases, lung disease, inflammation, and chronic alcohol consumption. Circulating oxidized phosphatidylcholine may also serve as a clinical biomarker. The focus of this review, therefore, will be to summarize existing evidence that oxidized phosphatidylcholine molecules play an important role in cardiovascular pathology.

[8] *Colantonio LD, Deng L, Chen L et al.* **Medical Expenditures Among Medicare Beneficiaries with Statin-Associated Adverse Effects Following Myocardial Infarction**. Cardiovascular drugs and therapy / sponsored by the International Society of Cardiovascular Pharmacotherapy 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30446883
ABSTRACT
PURPOSE: Compare medical expenditures among adults with statin-associated adverse effects (SAAE) and high statin adherence (HSA) following myocardial infarction (MI). METHODS: We analyzed expenditures in 2016 US dollars among Medicare beneficiaries with SAAE (n = 1741) and HSA (n = 55,567) who were >/= 66 years of age and initiated moderate/high-intensity statins following an MI in 2007-2013. SAAE were identified through a claims-based algorithm, which included down-titrating statins and initiating ezetimibe, switching to ezetimibe monotherapy, having a rhabdomyolysis or antihyperlipidemic adverse event followed by statin down-titration or discontinuation, or switching between >/= 3 statin types within 365 days following MI. HSA was defined by having a statin available to take for >/= 80% of the days in the 365 days following MI. RESULTS: Expenditures among beneficiaries with SAAE and HSA were $40,776 (95% CI $38,329-$43,223) and $26,728 ($26,482-$26,974), respectively, in the 365 days following MI, and $34,238 ($31,396-$37,080) and $29,053 ($28,605-$29,500), respectively, for

every year after the first 365 days. Multivariable-adjusted ratios comparing expenditures among beneficiaries with SAAE versus HSA in the first 365 days and after the first 365 days following MI were 1.51 (95% CI 1.43-1.59) and 1.23 (1.12-1.34), respectively. Inpatient and outpatient expenditures were higher among beneficiaries with SAAE versus HSA during and after the first 365 days following MI. Compared to beneficiaries with HSA, medication expenditures among those with SAAE were similar in the 365 days following MI, but higher afterwards. Other medical expenditures were higher among beneficiaries with SAAE versus HSA. CONCLUSION: SAAE are associated with increased expenditures following MI compared with HSA.

[9] *Hausenloy DJ, Chilian W, Crea F et al.* **The coronary circulation in acute myocardial ischaemia/reperfusion injury - a target for cardioprotection**. Cardiovascular research 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30428011
ABSTRACT
The coronary circulation is both culprit and victim of acute myocardial infarction. The rupture of an epicardial atherosclerotic plaque with superimposed thrombosis causes coronary occlusion, and this occlusion must be removed to induce reperfusion. However, ischaemia and reperfusion cause damage not only in cardiomyocytes but also in the coronary circulation, including microembolisation of debris and release of soluble factors from the culprit lesion, impairment of endothelial integrity with subsequently increased permeability and oedema formation, platelet activation and leukocyte adherence, erythrocyte stasis, a shift from vasodilation to vasoconstriction, and ultimately structural damage to the capillaries with eventual no-reflow, microvascular obstruction and intramyocardial haemorrhage. Therefore, the coronary circulation is a valid target for cardioprotection, beyond protection of the cardiomyocyte. Virtually all of the above deleterious endpoints have been demonstrated to be favourably influenced by one or the other mechanical or pharmacological cardioprotective intervention. However, no-reflow is still a serious complication of reperfused myocardial infarction and carries, independently from infarct size, an unfavourable prognosis. Microvascular obstruction and intramyocardial haemorrhage can be diagnosed by modern imaging technologies, but still await an effective therapy. The current review provides an overview of strategies to protect the coronary circulation from acute myocardial ischaemia/reperfusion injury. This article is part of a Cardiovascular Research Spotlight Issue entitled 'Cardioprotection Beyond the Cardiomyocyte', and emerged as part of the discussions of the European Union (EU)-CARDIOPROTECTION Cooperation in Science and Technology (COST) Action, CA16225.

[10] *Koskinas KC, Windecker S, Buhayer A et al.* **Design of the Randomized, Placebo-Controlled Evolocumab for Early Reduction of LDL-Cholesterol Levels in Patients with Acute Coronary Syndromes (EVOPACS) Trial**. Clinical cardiology 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30421481
ABSTRACT
Statins lower low-density lipoprotein cholesterol (LDL-C) and improve clinical outcomes in patients with atherosclerotic cardiovascular disease (CVD). Patients with acute coronary syndromes (ACS) often do not achieve LDL-C targets despite potent statin treatment, and have

a particularly high risk of early recurrent events. Evolocumab, a proprotein convertase subtilisin/kexin type (PCSK9)-inhibitor resulting in rapid, marked LDL-C reduction, has been studied in hypercholesterolemic subjects without CVD and stabilized patients with CVD; the feasibility, safety, and efficacy of this treatment initiated in the acute phase of ACS remain unknown. We report the design of Evolocumab for Early Reduction of LDL-Cholesterol Levels in Patients with ACS (EVOPACS), a phase-3, multicenter, randomized, double-blind, placebo-controlled trial to assess the feasibility, safety, and LDL-C-lowering efficacy of evolocumab on top of atorvastatin 40 mg in patients with ACS. The primary endpoint is percent change in LDL-C from baseline to 8 weeks. Secondary endpoints are adverse events and serious adverse events. Against a background of beneficial cardiovascular effects of statins beyond LDL-C lowering and in view of preclinical evidence of similar effects of PCSK9 inhibition, the study will also address a variety of exploratory endpoints including the change in C-reactive protein and other inflammatory biomarkers; platelet reactivity; and occurrence of contrast-induced acute kidney injury and myocardial injury in patients undergoing cardiac catheterization. An intracoronary imaging sub-study will assess the change from baseline in the lipid core burden index in non-culprit lesions, as assessed by serial near-infrared spectroscopy. Recruitment began in January 2018 and enrolment of 308 patients is planned.

[11] *Console L, Scalise M, Indiveri C.* **Exosomes in inflammation and role as biomarkers**. Clinica chimica acta; international journal of clinical chemistry 2018; 488:165-171.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30419221
ABSTRACT
Exosomes are endosomal-derived nano-vesicles. They are considered vehicles through which donor cells transfer proteins, lipids and nucleic acids to target cells thus influencing their metabolism. Exosomes are involved in inflammatory processes that play a pivotal role in a large number of pathologic states including cancer, inflammatory bowel diseases, type 2 diabetes, obesity, rheumatoid arthritis and neurodegenerative diseases. The association between inflammation and change in nature or expression level of some exosomal cargos is the fundamental step for identifying possible novel biomarkers of inflammatory-based diseases. A novel interesting exosome cargo is the SLC22A5 transport protein whose level in exosomes is regulated by the pro-inflammatory cytokine INF-gamma. The advantage of using exosomes as a biomarker vehicle consists of their ease of collection from body fluids such as urine and saliva as they may represent a non-invasive means for screening human pathology.

[12] *Oshakbayev K, Bimbetov B, Manekenova K et al.* **Severe nonalcoholic steatohepatitis and type 2 diabetes: liver histology after weight loss therapy in a randomized clinical trial**. Current medical research and opinion 2018:1-24.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30431378
ABSTRACT
OBJECTIVE: To evaluate the effectiveness of the fast weight loss method on liver steatosis, fibrosis, inflammation, glycemic and lipids features and body composition in patients with severe Nonalcoholic Steatohepatitis (NASH) and Type 2 Diabetes (T2D). METHODS: A 24-week open prospective randomised controlled clinical trial including 80 adult patients (aged 40-65

years) was performed. The patients after randomisation were divided in two groups: Main group followed the fast weight loss method; Control group received conventional drug treatment. The fast weight loss method included calorie restriction, salt intake, walking and sexual self-restraint. The conventional drug therapy included Vitamin E, Orlistat, Pioglitazone hydrochloride, Atorvastatin, Lisinopril, benzodiazepines and anti-inflammatory agents. Primary endpoints: ultrasound and histology suggestive of steatohepatitis, hepatic enzymes, weight loss, 2-hour oral glucose tolerance test, HbA1c. Secondary endpoints: blood pressure, lipids. RESULTS: 83% patients completed the study. In Main weight lost 7-16 kg (10-20% from baseline) for 8-10 weeks. In Main weight lost due to reduction of fat mass only. Main vs. Controls showed higher decrease in fat mass from baseline ($P < 0.001$). Ultrasound imaging and liver histological scoring system evidenced significant improvement on liver steatosis/fibrosis in Main ($P < 0.001$). In Main vs. Controls weight lost at 24 weeks led to positive laboratory changes in ALT, AST, 2-hour OGTT, HbA1c, HOMA-IR, BP, cholesterol, triglycerides, bilirubin total, blood hemoglobin ($P = 0.01$). The fast weight loss in the patients adequately led to decrease in symptomatic drugs up to complete abolition. CONCLUSIONS: The study showed benefits of the fast weight loss method improving in steatosis/fibrosis, biochemical/metabolic outcomes in patients with severe NASH and T2D.

[13] *Siskos D, Tziomalos K*. **The Role of Statins in the Management of Patients Undergoing Coronary Artery Bypass Grafting**. Diseases (Basel, Switzerland) 2018; 6.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30423861
ABSTRACT
Each year, a large number of patients undergo coronary artery bypass grafting surgery (CABG) worldwide. Accumulating evidence suggests that the preoperative administration of statins might be useful in preventing adverse events after CABG. In the present review, we discuss the role of statins in the perioperative management of patients undergoing CABG. Preoperative administration of statins in these patients substantially reduces the risk of postoperative atrial fibrillation and shortens hospital and intensive care unit (ICU) stay. Atorvastatin appears to be more effective, particularly when administered at high doses. Given these benefits and the safety of statins, their administration should be considered in patients undergoing CABG, even though the statins do not appear to affect the incidence of cardiovascular events and overall mortality perioperatively.

[14] *Rashid T, Nemazanyy I, Paolini C et al.* **Lipin1 deficiency causes sarcoplasmic reticulum stress and chaperone-responsive myopathy**. The EMBO journal 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30420558
ABSTRACT
As a consequence of impaired glucose or fatty acid metabolism, bioenergetic stress in skeletal muscles may trigger myopathy and rhabdomyolysis. Genetic mutations causing loss of function of the LPIN1 gene frequently lead to severe rhabdomyolysis bouts in children, though the metabolic alterations and possible therapeutic interventions remain elusive. Here, we show that lipin1 deficiency in mouse skeletal muscles is sufficient to trigger myopathy. Strikingly, muscle fibers display strong accumulation of both neutral and phospholipids. The metabolic lipid imbalance can be traced to an altered fatty acid synthesis and fatty acid oxidation,

accompanied by a defect in acyl chain elongation and desaturation. As an underlying cause, we reveal a severe sarcoplasmic reticulum (SR) stress, leading to the activation of the lipogenic SREBP1c/SREBP2 factors, the accumulation of the Fgf21 cytokine, and alterations of SR-mitochondria morphology. Importantly, pharmacological treatments with the chaperone TUDCA and the fatty acid oxidation activator bezafibrate improve muscle histology and strength of lipin1 mutants. Our data reveal that SR stress and alterations in SR-mitochondria contacts are contributing factors and potential intervention targets of the myopathy associated with lipin1 deficiency.

[15] *Hasegawa K*. **Cardiovascular Risk Management Targeting Inflammation in Addition to Lipid-lowering Therapy**. European cardiology 2017; 12:88.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30416560
ABSTRACT

[16] *Martinez-Rubio A, Freixa Pamias R*. **Key Recent Advances in Atherosclerosis Treatment with Modern Lipid-lowering Drugs: The New Frontier with PCSK9 Inhibitors**. European cardiology 2017; 12:30-32.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30416548
ABSTRACT

[17] *Ma L, Waldmann E, Ooi EMM et al.* **Lipoprotein(a) and Low-density lipoprotein apolipoprotein-B metabolism following apheresis in patients with elevated lipoprotein(a) and coronary artery disease**. European journal of clinical investigation 2018:e13053.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30447089
ABSTRACT
BACKGROUND: Lipoprotein apheresis effectively lowers lipoprotein(a) [Lp(a)] and low-density lipoprotein (LDL) by approximately 60-70%. The rebound of LDL and Lp(a) particle concentrations following lipoprotein apheresis allows the determination of fractional catabolic rate (FCR) and hence production rate (PR) during non-steady state conditions. We aimed to investigate the kinetics of Lp(a) and LDL apolipoprotein B-100 (apoB) particles in patients with elevated Lp(a) and coronary artery disease undergoing regular apheresis. PATIENTS AND METHODS: A cross-sectional study was carried out in 13 patients with elevated Lp(a) concentration (>500 mg/L) and coronary artery disease. Lp(a) and LDL-apoB metabolic parameters, including FCR and PR were derived by the fit of a compartment model to the Lp(a) and LDL-apoB concentration data following lipoprotein apheresis. RESULTS: The FCR of Lp(a) was significantly lower than that of LDL-apoB (0.39 (0.31, 0.49) vs 0.57 (0.46, 0.71) pools/day, P=0.03) with no significant differences in the corresponding PR (14.80 (11.34, 19.32) vs 15.73 (11.93, 20.75) mg/kg/day, P=0.80). No significant associations were observed between the FCR and PR of Lp(a) and LDL-apoB. CONCLUSIONS: In patients with elevated Lp(a), the fractional catabolism of Lp(a) is slower than that of LDL-apoB particles, implying that different metabolic pathways are involved in the catabolism of these lipoproteins. These findings have implications for new therapies for lowering apolipoprotein(a) and apoB to prevent atherosclerotic cardiovascular disease.

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[18] *Essers D, Schaublin M, Kullak-Ublick GA, Weiler S*. **Statin-associated immune-mediated necrotizing myopathy: a retrospective analysis of individual case safety reports from VigiBase**. Eur J Clin Pharmacol 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30430215
ABSTRACT
PURPOSE: Statins represent an effective treatment for hyperlipidaemia. Immune-mediated necrotising myopathy (IMNM), a form of statin myopathy, has recently been described, and is characterized by elevated creatine kinase, presence of antibodies against HMG-CoA and no improvement after drug discontinuation, even with immunosuppressive treatment. Information on IMNM is mainly from case reports and small case series. Therefore, all reported cases of IMNM in VigiBase, the WHO global database of individual case safety reports (ICSRs) including the underlying reporting patterns, were analysed to characterize more detailed this adverse drug reaction. METHODS: ICSRs of IMNM up to October 1, 2016 were extracted from VigiBase. Corresponding case narratives were requested from responsible national authorities to maximize the available data. The reports were analysed in terms of reporting criteria, co-reported terms, patient demographics, clinical data, administered medication, latency time, seriousness of the reaction and outcome. RESULTS: One hundred one deduplicated ICSRs of IMNM were reported from 17 countries until October 2016. Approximately two thirds of the cases were from the year 2016. Slightly more males than females were affected (52 [57%] males vs 39 [42%] females). Median reported patient age was 68 years (range 16 - 87 years). Ninety-one cases (99%) were classified as serious. Median latency time was 26 months (range 1 - 288 months). Median creatine kinase value was 6860 U/L (range 576 - 35,000 U/L). In total, eight patients (9%) had recovered from IMNM. Atorvastatin was the most frequently reported statin in 80% of cases. CONCLUSIONS: The number of IMNM reports has increased in recent years. IMNM associated with statin treatment seems to occur worldwide. Most IMNM cases were reported with atorvastatin. No dose dependency of statin-associated IMNM pathogenesis was identified.

[19] *Blauw LL, Noordam R, Soidinsalo S et al.* **Mendelian randomization reveals unexpected effects of CETP on the lipoprotein profile**. Eur J Hum Genet 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30420679
ABSTRACT
According to the current dogma, cholesteryl ester transfer protein (CETP) decreases high-density lipoprotein (HDL)-cholesterol (C) and increases low-density lipoprotein (LDL)-C. However, detailed insight into the effects of CETP on lipoprotein subclasses is lacking. Therefore, we used a Mendelian randomization approach based on a genetic score for serum CETP concentration (rs247616, rs12720922 and rs1968905) to estimate causal effects per unit (microg/mL) increase in CETP on 159 standardized metabolic biomarkers, primarily lipoprotein subclasses. Metabolic biomarkers were measured by nuclear magnetic resonance (NMR) in 5672 participants of the Netherlands Epidemiology of Obesity (NEO) study. Higher CETP concentrations were associated with less large HDL (largest effect XL-HDL-C, P = 6 x 10(-22)) and more small VLDL components (largest effect S-VLDL cholesteryl esters, P = 6 x 10(-6)). No causal effects were observed with LDL subclasses. All these effects were replicated in an independent cohort from European ancestry (MAGNETIC NMR GWAS; n ~20,000). Additionally, we assessed

observational associations between ELISA-measured CETP concentration and metabolic measures. In contrast to results from Mendelian randomization, observationally, CETP concentration predominantly associated with more VLDL, IDL and LDL components. Our results show that CETP is an important causal determinant of HDL and VLDL concentration and composition, which may imply that the CETP inhibitor anacetrapib decreased cardiovascular disease risk through specific reduction of small VLDL rather than LDL. The contrast between genetic and observational associations might be explained by a high capacity of VLDL, IDL and LDL subclasses to carry CETP, thereby concealing causal effects on HDL.

[20] *Hong Y, Park HB, Lee BK et al.* **Clinical feasibility of catheter-directed selective intracoronary computed tomography angiography using an extremely low dose of iodine in patients with coronary artery disease**. European radiology 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30421011
ABSTRACT
OBJECTIVE: This study aimed to evaluate the clinical feasibility of catheter-directed selective computed tomography angiography (S-CTA) in patients with coronary artery disease (CAD). METHODS: We prospectively enrolled 65 patients diagnosed with CAD who underwent conventional computed tomography angiography (C-CTA). C-CTA was performed with 60-90 mL of contrast medium (370 mg iodine/mL), whereas S-CTA was performed with 15 mL of contrast medium and 17.19 mg iodine/mL. Luminal enhancement range, homogeneity of luminal enhancement, image quality, plaque volume (PV), and percent aggregate plaque volume (%APV) were measured. Paired Student's t test, Wilcoxon rank-sum test, and Pearson's correlation coefficient were used to compare two methods. RESULTS: Luminal enhancement was significantly higher on S-CTA than on C-CTA (324.4 +/- 8.0 Hounsfield unit (HU) vs. 312.0 +/- 8.0 HU, $p < 0.0001$ in the per-vessel analysis). Transluminal attenuation gradient showed a significantly slower reduction pattern on S-CTA than on C-CTA (-0.65 HU/10 mm vs. -0.89 HU/10 mm, $p < 0.0001$ in the per-vessel analysis). Image noise was significantly lower on S-CTA than on C-CTA (39.6 +/- 10.0 HU vs. 43.9 +/- 9.4 HU, $p < 0.0001$). There was excellent correlation between S-CTA and C-CTA with respect to PV and %APV ($r = 0.99$, $r = 0.98$, respectively). CONCLUSIONS: S-CTA might be useful in facilitating atherosclerotic plaque analysis and providing guidance for complex lesions such as chronic total occlusion, particularly in cases in which on-site procedure planning is required. KEY POINTS: * Selective computed tomography angiography (S-CTA) can serve as an intraprocedural computed tomography angiography protocol. * S-CTA was performed with low dose of iodine compared with conventional computed tomography angiography. * S-CTA enables on-site atherosclerotic plaque analysis.

[21] *Guo X, Zhang T, Shi L et al.* **The relationship between lipid phytochemicals, obesity and its related chronic diseases**. Food & function 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30427004
ABSTRACT
The prevalence of obesity has received global attention in recent years, and lipid consumption has been considered as one of the direct reasons for obesity and related diseases. However, increasing evidence has indicated that edible vegetable oils could exert non-negligible physiological benefits in the daily diet, including suppression of appetite, lowering of blood

lipids, prevention of adipocyte synthesis, and reduction of inflammatory response. Bioactive phytochemicals in lipids and oils, such as tocopherol, phenolic compounds, and phytosterol, play an important role in these effects according to in vitro and in vivo studies. For these reasons, the present review focusses on minor bioactive components in oil and their anti-obesity effects, aiming to provide a systematic overview of the relationships between these minor components and obesity and related diseases.

[22] *Qu L, Li D, Gao X et al.* **Di'ao Xinxuekang Capsule, a Chinese Medicinal Product, Decreases Serum Lipids Levels in High-Fat Diet-Fed ApoE(-/-) Mice by Downregulating PCSK9**. Frontiers in pharmacology 2018; 9:1170.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30443213
ABSTRACT
Numerous risk factors are responsible for the development of atherosclerosis, for which an increased serum level of low-density lipoprotein cholesterol (LDL-C) is a driving force. By binding to the low-density lipoprotein cholesterol receptor (LDLR) and inducing LDLR degradation, proprotein convertase subtilisin/kexin type 9 (PCSK9) plays a key role in cholesterol homeostasis regulation. The inducement of PCSK9 expression is also an important reason for statin intolerance. The Di'ao Xinxuekang (DXXK) capsule extracted from Dioscorea nipponica Makino is a well-known traditional Chinese herbal medicinal product used in atherosclerotic cardiovascular disease. Although DXXK has been widely used in atherosclerotic cardiovascular treatment for nearly 30 years, studies on the potential mechanisms of the lipid-lowering effect are very limited. The purpose of the present study was to demonstrate the possible involvement of the PCSK9/LDLR signaling pathway in the lipid-lowering and antiatherosclerotic effect of DXXK in high-fat diet-fed ApoE(-/-) mice. The results showed that DXXK treatment alleviated hyperlipidemia, fat accumulation, and atherosclerosis formation in ApoE(-/-) mice. Furthermore, changes in the expression of PCSK9 mRNA in liver tissue and the circulating PCSK9 level in ApoE(-/-) mice were both reversed after DXXK treatment, and upregulation of LDLR in the liver was also detected in the protein level in DXXK-treated mice. Our study is the first to show that DXXK could alleviate lipid disorder and ameliorate atherosclerosis with downregulation of the PCSK9 in high-fat diet-fed ApoE(-/-) mice, suggesting that DXXK may be a potential novel therapeutic treatment and may support statin action in the treatment of atherosclerosis.

[23] *Albaugh VL, Banan B, Antoun J et al.* **Role of Bile Acids and GLP-1 in Mediating the Metabolic Improvements of Bariatric Surgery**. Gastroenterology 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30445014
ABSTRACT
BACKGROUND AND AIMS: Bile diversion to the ileum (GB-IL) has strikingly similar metabolic and satiating effects to Roux-en-Y gastric bypass (RYGB) in rodent obesity models. The metabolic benefits of these procedures are thought to be mediated by increased bile acids, though parallel changes in body weight and other confounding variables limits this interpretation. METHODS: Global G protein-coupled bile acid receptor-1 null (Tgr5(-/-)) and intestinal-specific farnesoid X receptor null (Fxr(Delta/E)) mice on high-fat diet as well as wild-type C57BL/6 and glucagon-like polypeptide 1 receptor deficient (Glp-1r(-/-)) mice on chow diet were

characterized following bile diversion to the ileum (GB-IL). RESULTS: GB-IL induced weight loss and improved oral glucose tolerance in HFD-fed Tgr5(-/-), but not Fxr(Delta/E) mice, suggesting a role for intestinal Fxr. GB-IL in wild-type, chow-fed mice prompted weight-independent improvements in glycemia and glucose tolerance secondary to augmented insulin responsiveness. Improvements were concomitant with increased levels of lymphatic GLP-1 in the fasted state and increased levels of intestinal Akkermansia muciniphila. Improvements in fasting glycemia after GB-IL were mitigated with Ex-9, a GLP-1 receptor antagonist, or cholestyramine, a bile acid sequestrant. The glucoregulatory effects of GB-IL were lost in whole body Glp-1r(-/-) mice. CONCLUSIONS: Bile diversion to the ileum improves glucose homeostasis via an intestinal Fxr-Glp-1 axis. Altered intestinal bile acid availability, independent of weight loss, and intestinal Akkermansia muciniphila appear to mediate the metabolic changes observed after bariatric surgery and might be manipulated for treatment of obesity and diabetes.

[24] *Jain V, Jana M, Upadhyay B et al.* **Prevalence, clinical & biochemical correlates of non-alcoholic fatty liver disease in overweight adolescents**. The Indian journal of medical research 2018; 148:291-301.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30425219
ABSTRACT
Background & objectives: Non-alcoholic fatty liver disease (NAFLD) characterized by excessive accumulation of fat in the liver, which can progress to inflammation, and cirrhosis, has emerged as an important complication of obesity in adults as well as children. This study was undertaken to assess the prevalence of NAFLD and its correlation with clinical and biochemical parameters in overweight Indian adolescents. Methods: In this cross-sectional study, 218 overweight adolescents aged 10 to 16 yr and their parents were included. Measurements included anthropometry, ultrasonography to diagnose NAFLD, fasting glucose, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and lipids for adolescents and parents, and additional parameters of blood pressure, body fat percentage (BF%), fasting insulin, apolipoprotein C3, tumour necrosis factor-alpha and adiponectin for adolescents. The variables were compared between adolescents with and without NAFLD, and logistic regression analysis was performed. Results: Mean age and body mass index (BMI)SD score (SDS) were 11.9+/-1.6 yr and 2.3+/-1.1, respectively. NAFLD was seen in 62.5 per cent of the adolescents. The prevalence of NAFLD in the parents was similar among the adolescents with and without NAFLD, while BMI and waist circumference SDS, BF per cent, blood pressure (BP), ALT, AST, insulin and homeostatic model assessment of insulin resistance (HOMA-IR) were significantly higher in the adolescents with NAFLD. On multiple logistic regression, abdominal obesity, HOMA-IR and BF per cent were independently associated with NAFLD with odds ratios (95% confidence interval) of 2.77 (1.40-5.47), 2.21 (1.16-4.21) and 2.17 (1.12-4.22), respectively. Interpretation & conclusions: NAFLD was noted among nearly two-thirds of the overweight adolescents. An independent association was observed between abdominal obesity, HOMA-IR and body fat percentage and NAFLD in overweight adolescents.

[25] *Angelidi AM, Stambolliu E, Adamopoulou KI, Kousoulis AA*. **Is Atorvastatin Associated with New Onset Diabetes or Deterioration of Glycemic Control? Systematic Review Using Data from 1.9 Million Patients**. Int J Endocrinol 2018; 2018:8380192.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30425742
ABSTRACT
Background: Current evidence indicates that statins increase the risk of new onset diabetes mellitus (NOD) and also deteriorate the glycemic control in patients with known diabetes mellitus (DM) after high-dose statin therapy. Aims: The aim of this review was to explore the effect of atorvastatin in causing NOD or deteriorating glycemic control in patients with DM. Methods: Two independent reviewers conducted the literature search, through PubMed database searching for articles published in English until April 2015, and only primary studies were included. Results: Of the 919 articles identified in our original search, 33 met the criteria for this review encompassing 1,951,113 participants. Twenty articles examined dysregulation of DM due to atorvastatin. Half of them showed that there was no significant change in glycemic control in patients treated with atorvastatin. Other studies showed that fasting plasma glucose and HbA1c levels were increased by atorvastatin. Thirteen articles examined if atorvastatin causes NOD. The majority of these articles showed that patients who used atorvastatin had a higher dose-dependent risk of developing NOD. Conclusion: This systematic review suggests that there is an association between atorvastatin treatment and NOD. Moreover, it showed that atorvastatin in high dose causes worsening of the glycemic control in patients with DM.

[26] *Su F, Shi M, Zhang J et al.* **Simvastatin Protects Heart from Pressure Overload Injury by Inhibiting Excessive Autophagy**. International journal of medical sciences 2018; 15:1508-1516.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30443172
ABSTRACT
Cardiac hypertrophy is an independent predictor of cardiovascular morbidity and mortality. To identify the mechanisms by which simvastatin inhibits cardiac hypertrophy induced by pressure overload, we determined effects of simvastatin on 14-3-3 protein expression and autophagic activity. Simvastatin was administered intragastrically to Sprague-Dawley (SD) rats before abdominal aortic banding (AAB). Neonatal rat cardiomyocytes (NRCs) were treated with simvastatin before angiotensin II (AngII) stimulation. 14-3-3, LC3, and p62 protein levels were determined by western blot. Autophagy was also measured by the double-labeled red fluorescent protein-green fluorescent protein autophagy reporter system. Simvastatin alleviated excessive autophagy, characterized by a high LC3II/LC3I ratio and low level of p62, and blunted cardiac hypertrophy while increasing 14-3-3 protein expression in rats that had undergone AAB. In addition, it increased 14-3-3 expression and inhibited excessive autophagy in NRCs exposed to AngII. Our study demonstrated that simvastatin may inhibit excessive autophagy, increase 14-3-3 expression, and finally exert beneficial effects on cardioprotection against pressure overload.

[27] *Ridker PM*. **Clinician's Guide to Reducing Inflammation to Reduce Atherothrombotic Risk: JACC Review Topic of the Week**. Journal of the American College of Cardiology 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30415883
ABSTRACT

Life-threatening cardiovascular events occur despite control of conventional risk factors. Inflammation, as measured by high-sensitivity C-reactive protein (hsCRP) concentration, is associated with future vascular events in both primary and secondary prevention, independent of usual risk markers. Statins are powerful lipid-lowering agents with clinically relevant anti-inflammatory effects. Recent data support targeting the interleukin (IL)-1-to-IL-6-to-CRP signaling pathway as an adjunctive method for atheroprotection. The CANTOS (Canakinumab Anti-inflammatory Thrombosis Outcomes Study) trial showed that reducing inflammation through IL-1beta inhibition significantly reduced vascular risk, beyond that achievable with lipid lowering. CANTOS further demonstrated a 31% reduction in cardiovascular mortality and all-cause mortality among patients treated with canakinumab who achieved the largest reductions in hsCRP, as well as efficacy in high-risk patients with chronic kidney disease and diabetes. This review outlines the clinical implications of CANTOS for patients with "residual inflammatory risk," the potential benefits and risks associated with anti-inflammatory therapy, and the importance of CANTOS for future drug development.

[28] *Wilson PWF, Polonsky TS, Miedema MD et al.* **Systematic Review for the 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines**. Journal of the American College of Cardiology 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30423394
ABSTRACT
BACKGROUND: The 2013 American College of Cardiology/American Heart Association guidelines for the treatment of blood cholesterol found little evidence to support the use of nonstatin lipid-modifying medications to reduce atherosclerotic cardiovascular disease (ASCVD) events. Since publication of these guidelines, multiple randomized controlled trials evaluating nonstatin lipid-modifying medications have been published. METHODS: We performed a systematic review to assess the magnitude of benefit and/or harm from additional lipid-modifying therapies compared with statins alone in individuals with known ASCVD or at high risk of ASCVD. We included data from randomized controlled trials with a sample size of >1,000 patients and designed for follow-up >1 year. We performed a comprehensive literature search and identified 10 randomized controlled trials for intensive review, including trials evaluating ezetimibe, niacin, cholesterol-ester transfer protein inhibitors, and PCSK9 inhibitors. The prespecified primary outcome for this review was a composite of fatal cardiovascular events, nonfatal myocardial infarction, and nonfatal stroke. RESULTS: The cardiovascular benefit of nonstatin lipid-modifying therapies varied significantly according to the class of medication. There was evidence for reduced ASCVD morbidity but not mortality with ezetimibe and 2 PSCK9 inhibitors. Reduced ASCVD mortality rate was reported for 1 PCSK9 inhibitor. The use of ezetimibe/simvastatin versus simvastatin in IMPROVE-IT (Improved Reduction of Outcomes: Vytorin Efficacy International Trial) reduced the primary outcome by 1.8% over 7 years (hazard ratio: 0.90; 95% CI: 0.84-0.96], 7-year number needed to treat: 56). The PSCK9 inhibitor evolocumab in the FOURIER study (Further Cardiovascular Outcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk) decreased the primary outcome by 1.5% over 2.2 years (hazard ratio: 0.80; 95% CI: 0.73-0.88; 2.2=year number needed to treat: 67). In ODYSSEY

OUTCOMES (Evaluation of Cardiovascular Outcomes After an Acute Coronary Syndrome During Treatment With Alirocumab), alirocumab reduced the primary outcome by 1.6% over 2.8 years (hazard ratio: 0.86; 95% CI: 0.79-0.93; 2.8-year number needed to treat: 63). For ezetimibe and the PSCK9 inhibitors, rates of musculoskeletal, neurocognitive, gastrointestinal, or other adverse event risks did not differ between the treatment and control groups. For patients at high risk of ASCVD already on background statin therapy, there was minimal evidence for improved ASCVD risk or adverse events with cholesterol-ester transfer protein inhibitors. There was no evidence of benefit for the addition of niacin to statin therapy. Direct comparisons of the results of the 10 randomized controlled trials were limited by significant differences in sample size, duration of follow-up, and reported primary outcomes. CONCLUSIONS: In a systematic review of the evidence for adding nonstatin lipid-modifying therapies to statins to reduce ASCVD risk, we found evidence of benefit for ezetimibe and PCSK9 inhibitors but not for niacin or cholesterol-ester transfer protein inhibitors.

[29] *Panich J, Gooden A, Shirazi FM, Malone DC*. **Warnings for drug-drug interactions in consumer medication information provided by community pharmacies**. Journal of the American Pharmacists Association : JAPhA 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30416068

ABSTRACT

OBJECTIVES: In 2006, the U.S. Food and Drug Administration (FDA) issued a draft guidance for pharmacies to provide consumer medication information (CMI) to patients receiving prescription medications. The objective of this study was to evaluate CMI leaflets provided by community pharmacies for accuracy and completeness regarding drug-drug interactions (DDIs). METHODS: CMI leaflets were obtained for 3 commonly prescribed medications (azithromycin, ciprofloxacin, and simvastatin) from 14 community pharmacies that are part of 6 chain organizations that operate in southern Arizona. Three to 4 salient interacting medications for each leaflet medication were identified with the use of 2 well recognized drug compendia. The content of the DDI information in the leaflets was evaluated for completeness. The font size and reading level of each leaflet were assessed as well. RESULTS: The CMI provided by 14 pharmacies appeared to be produced by 2 information vendors, Wolters Kluwer and First Databank. This was evident based on the identical wording and attribution (e.g., copyright statements) on the leaflets. The CMI from First Databank mentioned 5 of the 11 previously identified interactions with the target medications, although 1 chain in this group chose not to print the DDI section at all and as a result scored 0. The CMI developed by Wolters Kluwer mentioned only 2 of the 11 identified DDIs. The average reading grade level for First Databank leaflets was 10.6 (SD 2.87), and the reading level for the CMI from Wolters Kluwer was 5.0 (SD 1.02). The font sizes varied from 8 to 12 points; FDA recommends that the information be printed in 12-point size or larger. CONCLUSION: Community pharmacies appear to be distributing CMI leaflets with limited warnings about serious and well known DDIs. The results of this study suggest that consumers are not being informed through the CMI about important known DDIs.

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[30] *Atef MM, Hafez YM, Alshenawy HA, Emam MN*. **Ameliorative effects of autophagy inducer, simvastatin on alcohol-induced liver disease in a rat model**. Journal of cellular biochemistry 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30417426
ABSTRACT
Alcoholic liver disease (ALD) encompasses a variety of liver injuries with various underlying mechanisms but still no effective treatment. So we aimed to monitor the influence of simvastatin on alcohol-induced liver injury and elucidate the underlying mechanisms of its cytoprotective effect. Thirty male albino rats were randomly divided into five equal groups. Group 1 (control): received a standard diet; group 2: received simvastatin (10 mg kg(-1) day (-1)) once a day orally for 8 weeks; group 3: received 20% ethanol (7.9 g kg (-1) day (-1)) daily orally for 8 weeks; group 4: received 20% ethanol along with same simvastatin dose daily for 8 weeks; group 5: received 20% ethanol orally for 8 weeks then received the same simvastatin dose for the next 8 weeks. Serum alanine aminotransferase, aspartate aminotransferase, total cholesterol, triglycerides, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol were measured. Liver tissue malondialdehyde, reduced glutathione levels, and superoxide dismutase activity were estimated. B-cell lymphoma 2 and C/EBP homologous protein levels were evaluated by enzyme linked immunosorbent assay (ELISA). Light chain 3-II and peroxisome proliferation-activated receptor gamma messenger RNA expression was assessed by real-time polymerase chain reaction. Immunohistochemical staining was performed using anti-rat tumor necrosis factor-alpha antibody. Our results revealed that simvastatin treatment was able to ameliorate alcohol-induced liver damage; the improved biochemical data were confirmed by histopathological evaluation. Simvastatin being an autophagy inducer was able to prevent and reverse alcohol-induced liver changes via induction of autophagy, attenuation of oxidative stress, inflammation, and endoplasmic reticulum stress-induced apoptosis. Therefore, our findings suggest that treatment with simvastatin may be a useful approach in the management strategy of ALD.

[31] *Roy S, Vallepu S, Barrios C, Hunter K*. **Comparison of Comorbid Conditions Between Cancer Survivors and Age-Matched Patients Without Cancer**. Journal of clinical medicine research 2018; 10:911-919.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30425764
ABSTRACT
Background: Cancer survivors suffer from many comorbid conditions even after the cure of their cancers beyond 5 years. We explored the differences in the association of comorbid conditions between the cancer survivors and patients without cancer. Methods: Electronic medical records of 280 adult cancer survivors and 280 age-matched patients without cancer in our suburban internal medicine office were reviewed. Results: Mean age of the cancer survivors was 72.5 +/- 13.1 years, and the age of the patients without cancer was 72.5 +/- 12.8 years. The number of male cancer survivors was significantly higher than the female cancer survivors (52.5% vs. 47.5%, $P < 0.001$). There were significantly more Caucasians and other races (majority Asians) in the cancer survivor group compared to the patients without cancer group (81.8% vs. 79.3% and 4.6% vs. 0.4%, respectively, $P < 0.05$); while there were significantly less African Americans and Hispanics in the cancer survivor group compared to the patients without

cancer group (10.0% vs. 12.8% and 3.6% vs. 7.5%, respectively, P < 0.05). Hypertension (64.3%), hyperlipidemia (56.1%), osteoarthritis (34.3%), hypothyroidism (21.8%), diabetes mellitus (21.8%) and coronary artery disease (21.8%) were the most common comorbid conditions observed in the cancer survivors. Osteoarthritis was the only comorbid condition that was significantly less frequently associated with the cancer survivors compared to the patients without cancer (42.9%, P < 0.05). The frequencies of all other comorbid conditions were not significantly different between the two groups. The majority of our group of cancer survivors had one or more types of the top six cancers which include prostate cancer (30.7%), melanoma (13.9%), thyroid cancer (11.4%), colon cancer (11.1%), uterine cancer (11.1%) and urinary bladder cancer (11.1%); while only a few had cancer of the cervix (6.1%) or breast cancer (0.3%). Use of aspirin, statin, vitamin D, multivitamins, metformin and fish oil supplement in the cancer survivors was similar to the patients without cancer. Conclusions: Hypertension, hyperlipidemia, osteoarthritis, hypothyroidism, diabetes mellitus and coronary artery disease are the most common associated comorbid conditions in the cancer survivors. Osteoarthritis is less frequently seen in the cancer survivors compared to the patients without cancer. The frequencies of other comorbid conditions are not significantly different between the two groups.

[32] *Malguria N, Zimmerman S, Fishman EK*. **Coronary Artery Calcium Scoring: Current Status and Review of Literature**. Journal of computer assisted tomography 2018; 42:887-897.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30422915
ABSTRACT
Coronary artery calcium is a marker of overall atherosclerotic plaque burden, corresponding to approximately 20% overall atherosclerotic plaque burden. Coronary artery calcium screening, most commonly performed using the Agatston score, has been shown to be a predictor of future cardiovascular risk independent of conventional risk scores such as the Framingham risk score. Coronary artery calcium screening is also recommended on routine nongated, noncontrast chest computed tomography scans using several ordinal and visual scoring systems.

[33] *Bukiya AN, Blank PS, Rosenhouse-Dantsker A*. **Cholesterol intake and statin use regulate neuronal G protein-gated inwardly rectifying potassium channels**. Journal of lipid research 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30420402
ABSTRACT
Cholesterol, a critical component of the cellular plasma membrane, is essential for normal neuronal function. Cholesterol content is highest in the brain, where most cholesterol is synthesized de novo; HMG-CoA reductase controls the synthesis rate. Despite strict control, elevated blood cholesterol levels are common and are associated with various neurological disorders. G protein-gated inwardly rectifying potassium (GIRK) channels mediate the actions of inhibitory brain neurotransmitters. Loss of GIRK function enhances neuron excitability; gain of function reduces neuronal activity. However, the effect of dietary cholesterol or HMG-CoA reductase inhibition (i.e., statin therapy) on GIRK function remains unknown. Using a rat model, we compared the effects of a high-cholesterol versus normal diet both with and without

atorvastatin, a widely prescribed HMG-CoA reductase inhibitor, on neuronal GIRK currents. The high-cholesterol diet increased hippocampal CA1 region cholesterol levels and correspondingly increased neuronal GIRK currents. Both phenomena were reversed by cholesterol depletion in vitro. Atorvastatin countered the high-cholesterol diet effects on neuronal cholesterol content and GIRK currents; these effects were reversed by cholesterol enrichment in vitro. Our findings suggest that high-cholesterol diet and atorvastatin therapy affect ion channel function in the brain by modulating neuronal cholesterol levels.

[34] *Wang L, Zhou B, Zhou X et al.* **Combined lowering effects of rosuvastatin and L. acidophilus on cholesterol levels in rat**. Journal of microbiology and biotechnology 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30415528
ABSTRACT
Statins are a class of lipid lowering drugs commonly used in the prevention of cardiovascular diseases. However, statin therapy present many limitations, which lead to an increased interest in non-drug therapies, such as probiotics, to improve blood cholesterol levels. Indeed, probiotic strains such as Lactobacillus acidophilus have been found to improve blood lipid profiles, especially in reducing total cholesterol and LDL-C levels. In this study, we established a high-cholesterol rat model and studied the effect of Lactobacillus acidophilus administration alone or in conjunction with rosuvastatin. We were able to show that indeed Lactobacillus exerts a cholesterol-lowering effect. Additionally, we observed that when administered together, rosuvastin and Lactobacillus exert a combined cholesterol-lowering effect. Altogether, our data advocate for the possibility of establishing probiotics as non-drug supplements for the treatment of hypercholesterolemia.

[35] *Poon C, Gallo J, Joo J et al.* **Hybrid, metal oxide-peptide amphiphile micelles for molecular magnetic resonance imaging of atherosclerosis**. Journal of nanobiotechnology 2018; 16:92.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30442135
ABSTRACT
BACKGROUND: Atherosclerosis, a major source of cardiovascular disease, is asymptomatic for decades until the activation of thrombosis and the rupture of enlarged plaques, resulting in acute coronary syndromes and sudden cardiac arrest. Magnetic resonance imaging (MRI) is a noninvasive nuclear imaging technique to assess the degree of atherosclerotic plaque with high spatial resolution and excellent soft tissue contrast. However, MRI lacks sensitivity for preventive medicine, which limits the ability to observe the onset of vulnerable plaques. In this study, we engineered hybrid metal oxide-peptide amphiphile micelles (HMO-Ms) that combine an inorganic, magnetic iron oxide or manganese oxide inner core with organic, fibrin-targeting peptide amphiphiles, consisting of the sequence CREKA, for potential MRI imaging of thrombosis on atherosclerotic plaques. RESULTS: Hybrid metal oxide-peptide amphiphile micelles, consisting of an iron oxide (Fe-Ms) or manganese oxide (Mn-Ms) core with CREKA peptides, were self-assembled into 20-30 nm spherical nanoparticles, as confirmed by dynamic light scattering and transmission electron microscopy. These hybrid nanoparticles were found to be biocompatible with human aortic endothelial cells in vitro, and HMO-Ms bound to human clots three to five times more efficiently than its non-targeted counterparts. Relaxivity studies showed ultra-high r2 value of 457 mM(-1) s(-1) and r1 value of 0.48 mM(-1) s(-1) for Fe-Ms and

Mn-Ms, respectively. In vitro, MR imaging studies demonstrated the targeting capability of CREKA-functionalized hybrid nanoparticles with twofold enhancement of MR signals. CONCLUSION: This novel hybrid class of MR agents has potential as a non-invasive imaging method that specifically detects thrombosis during the pathogenesis of atherosclerosis.

[36] *Vinding RK, Stokholm J, Sevelsted A et al.* **Fish Oil Supplementation in Pregnancy Increases Gestational Age, Size for Gestational Age, and Birth Weight in Infants: A Randomized Controlled Trial**. The Journal of nutrition 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30418579
ABSTRACT
Background: Randomized trials have reported that supplementation with n-3 long-chain polyunsaturated fatty acids (LCPUFAs) in pregnancy can prolong pregnancy and thereby increase birth weight. Objective: We aimed to examine the relations of n-3 LCPUFA supplementation in pregnancy with duration of pregnancy, birth weight, and size for gestational age (GA). Methods: This was a double-blind randomized controlled trial conducted in 736 pregnant women and their offspring, from the Copenhagen Prospective Studies on Asthma in Childhood2010cohort. They were recruited between weeks 22 and 26 in pregnancy and randomly assigned to either of 2.4 g n-3 LCPUFA or control (olive oil) daily until 1 wk after birth. Exclusion criteria were endocrine, cardiovascular, or nephrologic disorders and vitamin D supplementation intake >600 IU/d. In this study we analyzed secondary outcomes, and further excluded twin pregnancies and extrauterine death. The primary outcome for the trial was persistent wheeze or asthma. Results: The random assignment ran between 2008 and 2010. Six hundred and ninety-nine mother-infant pairs were included in the analysis. n-3 LCPUFA compared with control was associated with a 2-d prolongation of pregnancy [median (IQR): 282 (275-288) d compared with 280 (273-286) d, P = 0.02], a 97-g higher birth weight (mean +/- SD: 3601 +/- 534 g compared with 3504 +/- 528 g, P = 0.02), and an increased size for GA according to the Norwegian population-based growth curves-Skjaerven (mean +/- SD: 49.9 +/- 28.3 percentiles compared with 44.5 +/- 27.6 percentiles, P = 0.01). Conclusion: Supplementing pregnant women with n-3 LCPUFAs during the third trimester is associated with prolonged gestation and increased size for GA, leading to a higher birth weight in this randomized controlled trial. This trial was registered at clinicaltrials.gov as NCT00798226.

[37] *Ferguson JF, Roberts-Lee K, Borcea C et al.* **Omega-3 polyunsaturated fatty acids attenuate inflammatory activation and alter differentiation in human adipocytes**. The Journal of nutritional biochemistry 2018; 64:45-49.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30428424
ABSTRACT
BACKGROUND: Omega-3 polyunsaturated fatty acids, specifically the fish-oil-derived eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), have been proposed as inflammation-resolving agents via their effects on adipose tissue. OBJECTIVE: We proposed to determine the effects of EPA and DHA on human adipocyte differentiation and inflammatory activation in vitro. METHODS: Primary human subcutaneous adipocytes from lean and obese subjects were treated with 100muM EPA and/or DHA throughout differentiation (differentiation studies) or for 72 h postdifferentiation (inflammatory studies). THP-1

monocytes were added to adipocyte wells for co-culture experiments. Subcutaneous and visceral adipose explants from obese subjects were treated for 72 h with EPA and DHA. Oil Red O staining was performed on live cells. Cells were collected for mRNA analysis by quantitative polymerase chain reaction, and media were collected for protein quantification by enzyme-linked immunosorbent assay. RESULTS: Incubation with EPA and/or DHA attenuated inflammatory response to lipopolysaccharide (LPS) and monocyte co-culture with reduction in post-LPS mRNA expression and protein levels of IL6, CCL2 and CX3CL1. Expression of inflammatory genes was also reduced in the endogenous inflammatory response in obese adipose. Both DHA and EPA reduced lipid droplet formation and lipogenic gene expression without alteration in expression of adipogenic genes or adiponectin secretion. CONCLUSIONS: EPA and DHA attenuate inflammatory activation of in vitro human adipocytes and reduce lipogenesis.

[38] *Han Q, Yeung SC, Ip MSM, Mak JCW*. **Dysregulation of cardiac lipid parameters in high-fat high-cholesterol diet-induced rat model**. Lipids in health and disease 2018; 17:255.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30428911
ABSTRACT
BACKGROUND: Lipid dysregulation is a classical risk factor for cardiovascular disease (CVD), yet scanty evidence existed regarding cardiac lipid metabolism that is directly related to heart damage. Recently, the relationship between dyslipidemia and pro-inflammatory insults has led to further understanding on the CVD-predisposing effects of dyslipidemia. The aims of the present study were to investigate whether high-fat high-cholesterol (HFHC) diet-induced hyperlipidemia would cause heart damage and to study the potential role of local cardiac lipid dysregulation in the occurrence of cellular injury. METHODS: Male Sprague-Dawley rats were divided into normal chow or HFHC diet groups, and sacrificed after 2 or 4 weeks, respectively. Lipid peroxidation marker level was measured. Lipid parameters in the rat hearts were detected. Cardiac damage was evaluated. RESULTS: HFHC diet increased serum levels of cholesterol and free fatty acids (FFAs) and led to systemic oxidative stress and pro-inflammatory status. Cardiac lipid dysregulation, which was characterized by elevated levels of cholesterol and adipocyte (A)- and heart (H)-fatty acid binding proteins (FABPs), occurred after HFHC diet for 4 weeks. Cardiac damage was further evident with elevated circulating H-FABP levels, increased cardiac interstitial fibrosis and the loss of troponin I. CONCLUSION: Our data demonstrated that HFHC diet led to systemic and cardiac lipid dysregulation, accompanied by systemic oxidative and pro-inflammatory stresses, and these may finally cooperate to cause a series of pathological changes of the heart tissue. Our findings suggest that maintenance of lipid regulation may be essential in the prevention of heart damage.

[39] *Xue EZ, Zhang MH, Liu CL*. **A pilot study of the effect of ezetimibe for postprandial hyperlipidemia**. Medicine (Baltimore) 2018; 97:e12960.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30431570
ABSTRACT
This study aimed to explore the feasible effect of ezetimibe for postprandial hyperlipidemia (PPHP).Sixty participants were included in this study. Of these, 30 subjects in the intervention group received ezetimibe, while the remaining 30 participants in the control group did not

undergo ezetimibe. All patients in intervention group were treated for a total of 2 weeks. Primary endpoints consisted of serum levels of total cholesterol (Total-C), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride (TG). Secondary endpoints included apoB-48, remnant lipoprotein cholesterol (RLP-C), blood glucose, insulin, hemoglobin A1c (HbA1c), and monocyte chemotactic protein (MCP). All outcomes were measured before and after 2-week treatment.After 2-week treatment, participants in the intervention group did not show better outcomes in primary endpoints of Total-C, LDL-C, HDL-C, and TG; and secondary endpoints of apoB-48, RLP-C, blood glucose, insulin, HbA1c, and MCP, compared with subjects in the control group.The results of this study showed that ezetimibe may be not efficacious for participants with PPHP after 2-week treatment.

[40] *Vekic J, Zeljkovic A, Stefanovic A et al.* **Obesity and dyslipidemia**. Metabolism 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30447223
ABSTRACT
Obesity, a pandemic of the modern world, is intimately associated with dyslipidemia, which is mainly driven by the effects of insulin resistance and pro-inflammatory adipokines. However, recent evidence suggests that obesity-induced dyslipidemia is not a unique pathophysiological entity, but rather has distinct characteristics depending on many individual factors. In line with that, in a subgroup of metabolically healthy obese (MHO) individuals, dyslipidemia is less prominent or even absent. In this review, we will address the main characteristics of dyslipidemia and mechanisms that induce its development in obesity. The fields, which should be further investigated to expand our knowledge on obesity-related dyslipidemia and potentially yield new strategies for prevention and management of cardiometabolic risk, will be highlighted. Also, we will discuss recent findings on novel lipid biomarkers in obesity, in particular proprotein convertase subtilisin/kexin type 9 (PCSK9), as the key molecule that regulates metabolism of low-density lipoproteins (LDL), and sphingosine-1-phosphate (S1P), as one of the most important mediators of high-density lipoprotein (HDL) particles function. Special attention will be given to microRNAs and their potential use as biomarkers of obesity-associated dyslipidemia.

[41] *Parhofer KG*. **[Lipidology - important changes of the last 10 years]**. MMW Fortschritte der Medizin 2018; 160:42-44.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30421198
ABSTRACT

[42] *Sabatine MS*. **PCSK9 inhibitors: clinical evidence and implementation**. Nature reviews. Cardiology 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30420622
ABSTRACT
The gene encoding PCSK9 was first identified and linked to the phenotype of familial hypercholesterolaemia approximately 15 years ago. Soon after, studies uncovered the role of PCSK9 in the regulation of LDL-receptor recycling and identified loss-of-function variants of PCSK9 that were associated with low circulating levels of LDL cholesterol (LDL-C) and a reduced

risk of coronary artery disease. With amazing rapidity, monoclonal antibodies against PCSK9 were developed and studied in large clinical programmes. These PCSK9 inhibitors lowered plasma LDL-C levels by approximately 60%, even in patients already receiving maximum-dose statin therapy. In the past year, three cardiovascular outcome trials were completed and showed that PCSK9 inhibitors significantly reduce the risk of major vascular events. Reassuringly, this benefit comes with no major offsetting adverse events, such as an excess of myalgias, elevation of hepatic aminotransferases levels in the plasma, incident diabetes mellitus or neurocognitive adverse events. The clinical benefit of PCSK9 inhibitors seen in these trials occurred in the setting of reducing LDL-C levels to unprecedentedly low levels, suggesting that more aggressive LDL-C targets should be adopted. New technologies to inhibit PCSK9 are now being harnessed and might further revolutionize our treatment of dyslipidaemia.

[43] *Akimoto H, Negishi A, Oshima S et al.* **Onset timing of statin-induced musculoskeletal adverse events and concomitant drug-associated shift in onset timing of MAEs**. Pharmacol Res Perspect 2018; 6:e00439.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30443347
ABSTRACT
To evaluate the onset timing of musculoskeletal adverse events (MAEs) that develop during statin monotherapy and to determine whether concomitant drugs used concurrently with statin therapy shifts the onset timing of MAEs. Cases in which statins (atorvastatin, rosuvastatin, simvastatin, lovastatin, fluvastatin, pitavastatin, and pravastatin) were prescribed were extracted from the US Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS) Data Files. The onset timing of MAEs during statin monotherapy was evaluated by determining the difference between statin start date and MAE onset date. The use of concomitant drugs with statin therapy was included in the analysis. Statins used in combination with concomitant drugs were compared with statin monotherapy to determine if the use of concomitant drugs shifted the onset timing of MAEs. The onset of MAEs was significantly faster with atorvastatin and rosuvastatin than with simvastatin. A difference in onset timing was not detected with other statins because the number of cases was too small for analysis. When evaluating concomitant drug use, the concomitant drugs that shifted the onset timing of MAEs could not be detected. Statins with strong low-density lipoprotein cholesterol-lowering effects (atorvastatin and rosuvastatin) contributed not only to a high risk of MAE onset, but also to a shorter time-to-onset. No concomitant drug significantly shifted the onset timing of MAEs when used concurrently with statins.

[44] *Xu S, Kamato D, Little PJ et al.* **Targeting epigenetics and non-coding RNAs in atherosclerosis: From mechanisms to therapeutics**. Pharmacology & therapeutics 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30439455
ABSTRACT
Atherosclerosis, the principal cause of cardiovascular death worldwide, is a pathological disease characterized by fibro-proliferation, chronic inflammation, lipid accumulation, and immune disorder in the vessel wall. As the atheromatous plaques develop into advanced stage, the vulnerable plaques are prone to rupture, which causes acute cardiovascular events, including ischemic stroke and myocardial infarction. Emerging evidence has suggested that

atherosclerosis is also an epigenetic disease with the interplay of multiple epigenetic mechanisms. The epigenetic basis of atherosclerosis has transformed our knowledge of epigenetics from an important biological phenomenon to a burgeoning field of cardiovascular research. Here, we provide a systematic and up-to-date overview of the current knowledge of three distinct but interrelated epigenetic processes (including DNA methylation, histone methylation/acetylation, and non-coding RNAs), in atherosclerotic plaque development and instability. Mechanistic and conceptual advances in understanding the biological roles of various epigenetic modifiers in regulating gene expression and functions of endothelial cells (vascular homeostasis, leukocyte adhesion, endothelial-mesenchymal transition, angiogenesis, and mechanotransduction), smooth muscle cells (proliferation, migration, inflammation, hypertrophy, and phenotypic switch), and macrophages (differentiation, inflammation, foam cell formation, and polarization) are discussed. The inherently dynamic nature and reversibility of epigenetic regulation, enables the possibility of epigenetic therapy by targeting epigenetic "writers", "readers", and "erasers". Several Food Drug Administration-approved small-molecule epigenetic drugs show promise in pre-clinical studies for the treatment of atherosclerosis. Finally, we discuss potential therapeutic implications and challenges for future research involving cardiovascular epigenetics, with an aim to provide a translational perspective for identifying novel biomarkers of atherosclerosis, and transforming precision cardiovascular research and disease therapy in modern era of epigenetics.

[45] *Yucel H, Yucel A, Arbag H et al.* **Effect of Statins on Hearing Function and Subjective Tinnitus in Hyperlipidemic Patients**. Romanian journal of internal medicine = Revue roumaine de medecine interne 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30447148
ABSTRACT
INTRODUCTION: It is known that hyperlipidemia reduces hearing functions. In this study, we aimed to study the effect of antihyperlipidemic drugs on hearing functions and tinnitus. METHODS: Eighty-four patients aged 18 to 84, who were diagnosed with hyperlipidemia and started treatment with the statin group (atorvastatin 20 mg and 40 mg, rosuvastatin 10 mg and 20 mg, and simvastatin 20 mg) of antihyperlipidemic drugs, were included in this study. All patients underwent pure-tone audiometry before starting treatment with antihyperlipidemic drugs. Patients with tinnitus were evaluated by Tinnitus Severity Index and Visual Analogue Scale. In the 6th month of the therapy, otologic examination, pure-tone audiometry and tinnitus evaluation of the patients were repeated. RESULTS: No significant difference was found in the pure-tone averages of the patients before and after statin use ($p>0.05$). However, it was found in the audiometry that, after statin use, all drugs caused to statistically significant decrease in the hearing thresholds at 6000 Hertz ($p<0.05$). Also, strongly increase was found in the Speech Discrimination percentages after treatment in patients using rosuvastatin 10 mg ($p= 0.022$). A significant decrease was found in the tinnitus frequency, duration, severity and degree of annoyance in patients using rosuvastatin 10 mg and 20 mg ($p<0.05$). CONCLUSION: Statin group of drugs can have a positive effect on the hearing functions and subjective tinnitus. In particular, it is seen that rosuvastatin group of statins has a more notable effect on tinnitus. It was considered that further studies with larger patient groups are needed.

[46] *Mehibel M, Ortiz-Martinez F, Voelxen N et al.* **Statin-induced metabolic reprogramming in head and neck cancer: a biomarker for targeting monocarboxylate transporters**. Scientific reports 2018; 8:16804.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30429503
ABSTRACT
Prognosis of HPV negative head and neck squamous cell carcinoma (HNSCC) patients remains poor despite surgical and medical advances and inadequacy of predictive and prognostic biomarkers in this type of cancer highlights one of the challenges to successful therapy. Statins, widely used for the treatment of hyperlipidaemia, have been shown to possess anti-tumour effects which were partly attributed to their ability to interfere with metabolic pathways essential in the survival of cancer cells. Here, we have investigated the effect of statins on the metabolic modulation of HNSCC cancers with a vision to predict a personalised anticancer therapy. Although, treatment of tumour-bearing mice with simvastatin did not affect tumour growth, pre-treatment for 2 weeks prior to tumour injection, inhibited tumour growth resulting in strongly increased survival. This was associated with increased expression of the monocarboxylate transporter 1 (MCT1) and a significant reduction in tumour lactate content, suggesting a possible reliance of these tumours on oxidative phosphorylation for survival. Since MCT1 is responsible for the uptake of mitochondrial fuels into the cells, we reasoned that inhibiting it would be beneficial. Interestingly, combination of simvastatin with AZD3965 (MCT1 inhibitor) led to further tumour growth delay as compared to monotherapies, without signs of toxicity. In clinical biopsies, prediagnostic statin therapy was associated with a significantly higher MCT1 expression and was not of prognostic value following conventional chemo-radiotherapy. These findings provide a rationale to investigate the clinical effectiveness of MCT1 inhibition in patients with HNSCC who have been taking lipophilic statins prior to diagnosis.

[47] Sizar O, Talati R. Ezetimibe. In: StatPearls. Treasure Island (FL): StatPearls Publishing StatPearls Publishing LLC.; 2018.
[48] Talreja O, Cassagnol M. Simvastatin. In: StatPearls. Treasure Island (FL): StatPearls Publishing
StatPearls Publishing LLC.; 2018.
[49] *Li RX, Apostolakis IZ, Kemper P et al.* **Pulse Wave Imaging in Carotid Artery Stenosis Human Patients in Vivo**. Ultrasound in medicine & biology 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30442386
ABSTRACT
Carotid stenosis involves narrowing of the lumen in the carotid artery potentially leading to a stroke, which is the third leading cause of death in the United States. Several recent investigations have found that plaque structure and composition may represent a more direct biomarker of plaque rupture risk compared with the degree of stenosis. In this study, pulse wave imaging was applied in 111 (n=11, N=13 plaques) patients diagnosed with moderate (>50%) to severe (>80%) carotid artery stenosis to investigate the feasibility of characterizing plaque properties based on the pulse wave-induced arterial wall dynamics captured by pulse wave imaging. Five (n=5 patients, N=20 measurements) healthy volunteers were also imaged as a control group. Both conventional and high-frame-rate plane wave radiofrequency imaging

sequences were used to generate piecewise maps of the pulse wave velocity (PWV) at a single depth along stenotic carotid segments, as well as intra-plaque PWV mapping at multiple depths. Intra-plaque cumulative displacement and strain maps were also calculated for each plaque region. The Bramwell-Hill equation was used to estimate the compliance of the plaque regions based on the PWV and diameter. Qualitatively, wave convergence, elevated PWV and decreased cumulative displacement around and/or within regions of atherosclerotic plaque were observed and may serve as biomarkers for plaque characterization. Intra-plaque mapping revealed the potential to capture wave reflections between calcified inclusions and differentiate stable (i.e., calcified) from vulnerable (i.e., lipid) plaque components based on the intra-plaque PWV and cumulative strain. Quantitatively, one-way analysis of variance indicated that the pulse wave-induced cumulative strain was significantly lower ($p < 0.01$) in the moderately and severely calcified plaques compared with the normal controls. As expected, compliance was also significantly lower in the severely calcified plaques regions compared with the normal controls ($p < 0.01$). The results from this pilot study indicated the potential of pulse wave imaging coupled with strain imaging to differentiate plaques of varying stiffness, location and composition. Such findings may serve as valuable information to compensate for the limitations of currently used methods for the assessment of stroke risk.

[50] *Ren S, Holliday E, Hure A et al.* **Pneumococcal polysaccharide vaccine associated with reduced lengths of stay for cardiovascular events hospital admissions: Experience from the Hunter Community Study**. Vaccine 2018; 36:7520-7524.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30420042

ABSTRACT

BACKGROUND: The pneumococcal polysaccharide vaccine (PPV) has been associated with reduced risk of cardiovascular events in human observational studies. Animal studies suggest that the phosphorylcholine epitope in the Streptococcus pneumoniae cell wall is structurally similar to oxidized low-density lipoprotein (oxLDL), hence PPV induces the production of antibodies that cross-react with anti-oxLDL and may cause regression of atherosclerotic plaque. We set out to determine the strength of association between PPV administration and reduction in cardiovascular events. METHODS: A longitudinal, population-based cohort study of older Australians, from the Hunter Community Study, with up to 11years of follow-up. We included participants aged>/=65years at baseline (2004-2008), without a history of cardiovascular disease (CVD). History of PPV administration at baseline was the main exposure of interest. "Total number of hospital bed-days with CVD primary diagnosis" was one of the main outcomes measured. Models were adjusted for age, diabetes, alcohol intake, and smoking status. Influenza vaccine was the control exposure used and fracture bed-days was the control outcome used, to investigate the potential for residual confounding. RESULTS: 91 of the total 1074 participants (mean age=72, male=45%) experienced a CVD event during follow-up. PPV (regardless of influenza vaccine) was associated with a significant reduction in CVD bed-day, (n=863, incident rate ratio, IRR=0.65, 95%CI: 0.45-0.94, p=0.02), but influenza vaccine (regardless of PPV) was not (n=864, IRR=0.86, 95%CI: 0.54-1.35, p=0.51). Furthermore, PPV adjusted for influenza vaccine remained associated with CVD bed-days (IRR=0.64, 95%CI: 0.43-0.96, p=0.03) but was not associated with fracture bed-days (IRR=0.75, 95%CI: 0.28-2.00, p=0.56). CONCLUSION: PPV demonstrated a 35% reduction in CVD bed-days. This finding was

robust to residual confounding, using a control exposure and a control outcome, eliminating the concern for healthy-user bias. A large double-blinded placebo-controlled RCT is underway to confirm our finding and to explore the proposed mechanism of action (ACTRN12615000536561).