[1] *Sobati S, Shakouri A, Edalati M et al.* **PCSK9: A Key Target for the Treatment of Cardiovascular Disease (CVD)**. Advanced pharmaceutical bulletin 2020; 10:502-511.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33062601

ABSTRACT

Proprotein convertase subtilisin/kexin type 9 (PCSK9), as a vital modulator of low-density lipoprotein cholesterol (LDL-C) , is raised in hepatocytes and released into plasma where it binds to LDL receptors (LDLR), leading to their cleavage. PCSK9 adheres to the epidermal growth factor-like repeat A (EGF-A) domain of the LDLR which is confirmed by crystallography. LDLR expression is adjusted at the transcriptional level through sterol regulatory element binding protein 2 (SREBP-2) and at the post translational stages, specifically through PCSK9, and the inducible degrader of the LDLR PCSK9 inhibition is an appealing new method for reducing the concentration of LDL-C. In this review the role of PCSK9 in lipid homeostasis was elucidated, the effect of PCSK9 on atherosclerosis was highlighted, and contemporary therapeutic techniques that focused on PCSK9 were summarized. Several restoration methods to inhibit PCSK9 have been proposed which concentrate on both extracellular and intracellular PCSK9, and they include blockage of PCSK9 production by using gene silencing agents and blockage of it's binding to LDLR through antibodies and inhibition of PCSK9 autocatalytic processes by tiny molecule inhibitors.

[2] *Rissetti G, Zeni D, Ongaratti BR et al.* **Lipid profile and response to statin therapy in patients with hypopituitarism**. Archives of endocrinology and metabolism 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33049128

ABSTRACT

OBJECTIVE: Dyslipidemia is prevalent among patients with hypopituitarism, especially in those with growth hormone (GH) deficiency. This study aimed to evaluate the response to statin therapy among adult patients with dyslipidemia and hypopituitarism. METHODS: A total of 113 patients with hypopituitarism following up at a neuroendocrinology unit were evaluated for serum lipid levels. Dyslipidemia was diagnosed in 72 (63.7%) of these patients. A control group included 57 patients with dyslipidemia and normal pituitary function. The distribution of gender, age, weight, and dyslipidemia type was well balanced across both groups, and all participants were treated with simvastatin at doses adjusted to obtain normal lipid levels. RESULTS: Patients with hypopituitarism and dyslipidemia presented deficiency of TSH (69%), gonadotropins (69%), ACTH (64%), and GH (55%) and had a similar number of deficient pituitary axes compared with patients with hypopituitarism but without dyslipidemia. All patients with dyslipidemia (with and without hypopituitarism) had lipid levels well controlled with doses of simvastatin ranging from 20-40 mg/day. The mean daily dose of simvastatin was not significantly different between patients with and without hypopituitarism (26.7 versus 23.5 mg, $p = 0.10$). Similarly, no significant variation in simvastatin dose was observed between patients with different causes of hypopituitarism, presence or absence of GH deficiency, number of deficient pituitary axes, prior pituitary radiation therapy or not, and presence or absence of obesity. CONCLUSION: Patients with GH deficiency without GH replacement showed good response to simvastatin at a mean dose equivalent to that used in individuals with dyslipidemia and normal pituitary function.

[3] *Nishimiya K, Matsumoto Y, Shimokawa H*. **Recent Advances in Vascular Imaging**. Arteriosclerosis, thrombosis, and vascular biology 2020:Atvbaha120313609.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33054393

ABSTRACT

Recent advances in vascular imaging have enabled us to uncover the underlying mechanisms of vascular diseases both ex vivo and in vivo. In the past decade, efforts have been made to establish various methodologies for evaluation of atherosclerotic plaque progression and vascular inflammatory changes in addition to biomarkers and clinical manifestations. Several recent publications in Arteriosclerosis, Thrombosis, and Vascular Biology highlighted the essential roles of in vivo and ex vivo vascular imaging, including magnetic resonance image, computed tomography, positron emission tomography/scintigraphy, ultrasonography, intravascular ultrasound, and most recently, optical coherence tomography, all of which can be used in bench and clinical studies at relative ease. With new methods proposed in several landmark studies, these clinically available imaging modalities will be used in the near future. Moreover, future development of intravascular imaging modalities, such as optical coherence tomography-intravascular ultrasound, optical coherence tomography-near-infrared autofluorescence, polarized-sensitive optical coherence tomography, and micro-optical coherence tomography, are anticipated for better management of patients with cardiovascular disease. In this review article, we will overview recent advances in vascular imaging and ongoing works for future developments.

[4] *Kong Q, Liu M, Li Y et al.* **Effect of evolocumab on the progression and stability of atherosclerotic plaques as evaluated by grayscale and iMAP-IVUS**. Ann Palliat Med 2020; 9:3078-3088.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33065780

ABSTRACT

BACKGROUND: Evolocumab inhibits the proprotein convertase subtilisin/kexin type 9 protein and is a potent cholesterol-lowering drug. However, the relationship between evolocumab and inflammation, and the effects of evolocumab on the stability of atherosclerotic plaques remain unknown. METHODS: Twenty-seven purebred New Zealand rabbits were fed with an atherogenic diet for 2 weeks. The abdominal aortic endothelium was balloon-injured. The rabbits were divided into the atorvastatin (2 mg/kg/day; Ato), evolocumab (7 mg/kg/2 weeks, Evo) and control groups. Intravascular ultrasound (IVUS) images of the abdominal artery were analyzed at 10 and 18 weeks. Additionally, the serum levels of the biomarkers were measured at baseline, and at 10 and 18 weeks. RESULTS: The serum levels of triglycerides, total cholesterol, low-density lipoprotein cholesterol (LDL-C), and monocyte chemoattractant protein-1 (MCP-1) increased after 10 weeks of administration of the proatherosclerotic diet, while the levels of high-density lipoprotein cholesterol (HDL-C) and transforming growth factor-β (TGF-β) decreased. The reduction in the serum levels of triglycerides, total cholesterol, LDL-C, MCP-1, TGF-β, and toll-like receptor 4 (TLR4) following treatment with evolocumab was higher than that of atorvastatin. Both evolocumab and atorvastatin reduced the percent atheroma volume. Evolocumab increased the fibrotic% and decreased the necrotic%. Correlation analysis revealed that the levels of triglycerides, total cholesterol, LDL-C, MCP-1, TGF-β, and TLR4 were negatively correlated with the fibrotic%, but were positively correlated with the necrotic%. Multivariate linear regression analysis revealed that treatment with atorvastatin, and especially evolocumab, was a consistent predictor of the percent atheroma volume, and fibrotic and necrotic composition. CONCLUSIONS: Proprotein convertase subtilisin/kexin type 9 regulates the serum levels of lipid and cholesterol may via inflammatory

pathways. The results also indicate that evolocumab is more potent than atorvastatin in suppressing the progression and stability of atherosclerotic plaque in rabbits.

[5] *Gong J, Wang HX, Lao YH et al.* **A Versatile Nonviral Delivery System for Multiplex Gene-Editing in the Liver**. Adv Mater 2020:e2003537.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33053221
ABSTRACT
Recent advances in CRISPR present attractive genome-editing toolsets for therapeutic strategies at the genetic level. Here, a liposome-coated mesoporous silica nanoparticle (lipoMSN) is reported as an effective CRISPR delivery system for multiplex gene-editing in the liver. The MSN provides efficient loading of Cas9 plasmid as well as Cas9 protein/guide RNA ribonucleoprotein complex (RNP), while liposome-coating offers improved serum stability and enhanced cell uptake. Hypothesizing that loss-of-function mutation in the lipid-metabolism-related genes pcsk9, apoc3, and angptl3 would improve cardiovascular health by lowering blood cholesterol and triglycerides, the lipoMSN is used to deliver a combination of RNPs targeting these genes. When targeting a single gene, the lipoMSN achieved a 54% gene-editing efficiency, besting the state-of-art Lipofectamine CRISPRMax. For multiplexing, lipoMSN maintained significant gene-editing at each gene target despite reduced dosage of target-specific RNP. By delivering combinations of targeting RNPs in the same nanoparticle, synergistic effects on lipid metabolism are observed in vitro and vivo. These effects, such as a 50% decrease in serum cholesterol after 4 weeks of post-treatment with lipoMSN carrying both pcsk9 and angptl3-targeted RNPs, could not be reached with a single gene-editing approach. Taken together, this lipoMSN represents a versatile platform for the development of efficient, combinatorial gene-editing therapeutics.

[6] *Gibson CM, Kastelein JJP, Phillips AT et al.* **Rationale and design of ApoA-I Event Reducing in Ischemic Syndromes II (AEGIS-II): A phase 3, multicenter, double-blind, randomized, placebo-controlled, parallel-group study to investigate the efficacy and safety of CSL112 in subjects after acute myocardial infarction**. American heart journal 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33065120
ABSTRACT
Acute myocardial infarction (MI) patients remain at high risk for recurrent events. Cholesterol efflux, mediated by apolipoprotein A-I, removes excess cholesterol from atherosclerotic plaque and transports it to the liver for excretion. Impaired cholesterol efflux is associated with higher cardiovascular (CV) event rates among both patients with stable coronary artery disease and recent MI. CSL112, a novel intravenous formulation of apolipoprotein A-I (human) derived from human plasma, increases cholesterol efflux capacity. AEGIS-II is a phase 3, multicenter, double-blind, randomized, placebo-controlled, parallel-group trial investigating the efficacy and safety of CSL112 compared to placebo among high-risk acute MI participants. Eligibility criteria include age ≥ 18 years with type 1 (spontaneous) MI, evidence of multivessel stable coronary artery disease, and presence of diabetes requiring pharmacotherapy, or ≥2 of the following: age ≥ 65 years, prior MI, or peripheral artery disease. A target sample of 17,400 participants will be randomized 1:1 to receive 4 weekly infusions of CSL112 6 g or placebo, initiated prior to or on the day of discharge and within 5 days of first medical contact. The primary outcome is the time to first occurrence of the composite of CV death, MI, or stroke through 90 days. Key

secondary outcomes include the total number of hospitalizations for coronary, cerebral, or peripheral ischemia through 90 days and time to first occurrence of the composite primary outcome through 180 and 365 days. AEGIS-II will be the first trial to formally test whether enhancing cholesterol efflux can reduce the rate of recurrent major adverse CV events.

[7] *Crisóstomo L, Videira RA, Jarak I et al.* **Diet during early life defines testicular lipid content and sperm quality in adulthood**. American journal of physiology. Endocrinology and metabolism 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33044846
ABSTRACT
Childhood obesity is a serious concern associated with ill health later in life. Emerging data suggest that obesity has long-term adverse effects upon male sexual and reproductive health but few studies addressed this issue. We hypothesized that exposure to high-fat diet during early life alters testicular lipid content and metabolism leading to permanent damage to sperm parameters. After weaning (day 21 after birth), 36 male mice were randomly divided into 3 groups and fed with different diet regimen for 200 days: CTRL-standard chow; HFD-high-fat diet (Carbohydrate: 35.7%, Protein: 20.5%, Fat: 36.0%); HFDt-high-fat diet for 60 days then replaced by standard chow. Biometric and metabolic data were monitored. Animals were then sacrificed, and tissues collected. Epididymal sperm parameters and endocrine parameters were evaluated. Testicular metabolites were extracted and characterized by 1H-NMR and GC-MS. Testicular mitochondrial and antioxidant activity were evaluated. Our results show that mice fed with high-fat diet, even if only until early adulthood, had lower sperm viability and motility, and higher incidence of head and tail defects. Although diet reversion with weight loss during adulthood prevents the progression of metabolic syndrome, testicular content in fatty acids is irreversibly affected. Excessive fat intake promoted an over-accumulation of pro-inflammatory n-6 polyunsaturated fatty acids in testis, which are strongly correlated with negative effects upon sperm quality. Therefore, the adoption of high-fat diets during early life correlates to irreversible changes in testicular lipid content and metabolism, which are related to permanent damage to sperm quality later in life.

[8] *Cherubini JM, Cheng JL, Williams JS, MacDonald MJ*. **Sleep deprivation and endothelial function: reconciling seminal evidence with recent perspectives**. American journal of physiology. Heart and circulatory physiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33064569
ABSTRACT
Sleep is critical for the maintenance of physiological homeostasis and, as such, inadequate sleep beckons a myriad of pathologies. Sleep deprivation is a growing health concern in contemporary society since short sleep durations are associated with increased cardiovascular disease risk and atherosclerotic plaque development. Vascular endothelial dysfunction is an antecedent to atherosclerosis and cardiovascular disease. Herein, we review seminal literature indicating short sleep durations attenuate endothelial function and explore more recent evidence indicating that sleep deprivation perturbs autonomic balance and the circadian rhythmicity of peripheral vascular clock components. We further examine literature that indicates a mechanistic link between short sleep and endothelial dysfunction and subsequent morbidity. Understanding the mechanisms that regulate endothelial function in the context of sleep deprivation facilitates the development and optimization of interventions, such as

exercise, that mitigate the ramifications of inadequate sleep on vascular function and cardiovascular and health.

[9] *Song EJ, Ahn S, Min SK et al.* **Combined application of rapamycin and atorvastatin improves lipid metabolism in apolipoprotein E-deficient mice with chronic kidney disease**. BMB reports 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33050984
ABSTRACT
Atherosclerosis arising from the pro-inflammatory conditions associated with chronic kidney disease (CKD) increases major cardiovascular morbidity and mortality. Rapamycin (RAPA) is known to inhibit atherosclerosis under CKD and non-CKD conditions, but it can cause dyslipidemia; thus, the co-application of lipid-lowering agents is recommended. Atorvastatin (ATV) has been widely used to reduce serum lipids levels, but its synergistic effect with RAPA in CKD remains unclear. Here, we analyzed the effect of their combined treatment on atherosclerosis stimulated by CKD in apolipoprotein E-deficient (ApoE-/-) mice. Oil Red O staining revealed that treatment with RAPA and RAPA+ATV, but not ATV alone, significantly decreased the atherosclerotic lesions in the aorta and aortic sinus, compared to those seen in the control (CKD) group. The co-administration of RAPA and ATV improved the serum lipid profile and raised the expression levels of proteins involved in reverse cholesterol transport (LXRα, CYP7A1, ABCG1, PPARγ, ApoA1) in the liver. The CKD group showed increased levels of various genes encoding atherosclerosis-promoting cytokines in the spleen (Tnf-α, Il-6 and Il-1β) and aorta (Tnf-α and Il-4), and these increases were attenuated by RAPA treatment. ATV and RAPA+ATV decreased the levels of Tnf-α and Il-1β in the spleen, but not in the aorta. Together, these results indicate that, in CKD-induced ApoE-/- mice, RAPA significantly reduces the development of atherosclerosis by regulating the expression of inflammatory cytokines and the co-application of ATV improves lipid metabolism.

[10] *Simha V*. **Management of hypertriglyceridemia**. Bmj 2020; 371:m3109.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33046451
ABSTRACT
Hypertriglyceridemia is one of the most common lipid abnormalities encountered in clinical practice. Many monogenic disorders causing severe hypertriglyceridemia have been identified, but in most patients triglyceride elevations result from a combination of multiple genetic variations with small effects and environmental factors. Common secondary causes include obesity, uncontrolled diabetes, alcohol misuse, and various commonly used drugs. Correcting these factors and optimizing lifestyle choices, including dietary modification, is important before starting drug treatment. The goal of drug treatment is to reduce the risk of pancreatitis in patients with severe hypertriglyceridemia and cardiovascular disease in those with moderate hypertriglyceridemia. This review discusses the various genetic and acquired causes of hypertriglyceridemia, as well as current management strategies. Evidence supporting the different drug and non-drug approaches to treating hypertriglyceridemia is examined, and an easy to adopt step-by-step management strategy is presented.

[11] *Rahhal A, Khir F, Aljundi AH et al.* **Clinical outcomes of high-intensity doses of atorvastatin in patients with acute coronary syndrome: A retrospective cohort study using real-world data**. British journal of clinical pharmacology 2020.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33068036

ABSTRACT

AIMS: To compare the effectiveness and safety of 2 high-intensity atorvastatin doses (40 mg vs 80 mg) among acute coronary syndrome (ACS) patients. METHODS: This retrospective observational cohort study using real-world data included patients admitted with ACS to the Heart Hospital in Qatar between 1 January 2017 and 31 December 2018. The primary endpoint was a composite of cardiovascular disease-associated death, nonfatal ACS and nonfatal stroke. Cox proportional hazard regression analysis was used to determine the association between the 2 high-intensity atorvastatin dosing regimens and the primary outcome at 1 month and 12 months postdischarge. RESULTS: Of the 626 patients included in the analyses, 475 (75.9%) received atorvastatin 40 mg, while 151 (24.1%) received atorvastatin 80 mg following ACS. Most of the patients were Asian (73%), male (97%) with a mean age of 50 years and presented with ST-elevation myocardial infarction (60%). The incidence of the primary effectiveness outcome did not differ between the atorvastatin 40-and 80-mg groups at 1 month (0.8 vs 1.3%; adjusted hazard ratio = 0.59, 95% confidence interval 0.04-8.13, P = .690) and at 12 months (3.2 vs 4%; adjusted hazard ratio = 0.57, 95% confidence interval 0.18-1.80, P = .340). Similarly, the use of the 2 doses of atorvastatin resulted in comparable safety outcomes, including liver toxicity, myopathy and rhabdomyolysis with an event rate of <1% in both groups. CONCLUSION: The use of atorvastatin 40 mg in comparison to atorvastatin 80 mg in patients with ACS resulted in similar cardiovascular effectiveness and safety outcomes.

[12] *Padgett LE, Dinh HQ, Wu R et al.* **Naive CD8(+) T Cells Expressing CD95 Increase Human Cardiovascular Disease Severity**. Arteriosclerosis, thrombosis, and vascular biology 2020:Atvbaha120315106.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33054398

ABSTRACT

OBJECTIVE: Cardiovascular disease (CVD) remains a significant global health concern with a high degree of mortality. While CD4(+) T cells have been extensively studied in CVD, the importance of CD8(+) T cells in this disease, despite their abundance and increased activation in human atherosclerotic plaques, remains largely unknown. To compare the peripheral T-cell signatures between humans with a high (severe) risk of CVD (including myocardial infarction or stroke) to those with a low risk of CVD. Approach and Results: Using mass cytometry, we uncovered a naive CD8(+) T (T(N)) cell population expressing CD95 (termed CD95(+)CD8(+) stem cell memory T [CD8 T(SCM)] cells) that was enriched in patients with high compared with low CVD. This T-cell subset enrichment within individuals with high CVD was a relative increase and resulted from the loss of CD95(lo) cells within the T(N) compartment. We found that CD8 T(SCM) cells positively correlated with CVD risk in humans, while CD8(+) T(N) cells were inversely correlated. Atherosclerotic apolipoprotein E-deficient (ApoE(-/-)) mice also displayed respective 7- and 2-fold increases in CD8(+) T(SCM) frequencies within the peripheral blood and aorta-draining paraaortic lymph nodes compared with C57BL/6J mice. CD8(+) T(SCM) cells were 1.7-fold increased in aortas from western diet fed ApoE(-/-) mice compared with normal laboratory diet-fed ApoE(-/-) mice. Importantly, transfer of T(SCM) cells into immune-deficient Rag.Ldlr recipient mice that lacked T cells increased atherosclerosis, illustrating the importance of these cells in atherogenesis. CONCLUSIONS: CD8(+) T(SCM)

cells are increased in humans with high CVD. As these T(SCM) cells promote atherosclerosis, targeting them may attenuate atherosclerotic plaque progression.

[13] *Motkowski R, Maciejczyk M, Hryniewicka M et al.* **Effect of Statin Therapy on the Plasma Concentrations of Retinol, Alpha-Tocopherol and Coenzyme Q10 in Children with Familial Hypercholesterolemia**. Cardiovascular drugs and therapy / sponsored by the International Society of Cardiovascular Pharmacotherapy 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33052507
ABSTRACT
PURPOSE: Familial hypercholesterolemia (FH) requires early treatment. However, statins, which are regarded the first-line therapy, have an influence on redox balance. Antioxidant vitamins are important for many metabolic processes in the developing body. There are few data available on the long-term safety of statin use in children. The aim of this study was to evaluate the influence of statin treatment in children with FH on plasma concentrations of antioxidant vitamins: retinol, alpha-tocopherol and coenzyme Q10. METHODS: The first study group consisted of 13 children aged 10-18 years treated with simvastatin for at least 6 months, and the second group comprised 13 age- and sex-matched children with hypercholesterolemia, in whom pharmacological treatment had not been applied yet. Analyses were performed using a high-performance liquid chromatograph coupled with a MS detector. RESULTS: The analysis did not reveal significant differences in the concentration of retinol, alpha-tocopherol or coenzyme Q10 between the studied groups. The adjustment of the concentrations of the vitamins to the cholesterol level also indicated no significant differences. We found no deficits in antioxidant vitamins in patients treated with statins, or any risk of adverse effects associated with an increase in their concentration. CONCLUSION: There is no rationale for additional supplementation using antioxidant vitamins or modification of low-fat and low-cholesterol diet in pediatric patients treated with statins.

[14] *Iqbal Z, Ho JH, Adam S et al.* **Managing hyperlipidaemia in patients with COVID-19 and during its pandemic: An expert panel position statement from HEART UK**. Atherosclerosis 2020; 313:126-136.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33045618
ABSTRACT
The emergence of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which causes Coronavirus Disease 2019 (COVID-19) has resulted in a pandemic. SARS-CoV-2 is highly contagious and its severity highly variable. The fatality rate is unpredictable but is amplified by several factors including advancing age, atherosclerotic cardiovascular disease, diabetes mellitus, hypertension and obesity. A large proportion of patients with these conditions are treated with lipid lowering medication and questions regarding the safety of continuing lipid-lowering medication in patients infected with COVID-19 have arisen. Some have suggested they may exacerbate their condition. It is important to consider known interactions with lipid-lowering agents and with specific therapies for COVID-19. This statement aims to collate current evidence surrounding the safety of lipid-lowering medications in patients who have COVID-19. We offer a consensus view based on current knowledge and we rated the strength and level of evidence for these recommendations. Pubmed, Google scholar and Web of Science were searched extensively for articles using search terms: SARS-CoV-2, COVID-19, coronavirus, Lipids, Statin, Fibrates, Ezetimibe, PCSK9 monoclonal

antibodies, nicotinic acid, bile acid sequestrants, nutraceuticals, red yeast rice, Omega-3-Fatty acids, Lomitapide, hypercholesterolaemia, dyslipidaemia and Volanesorsen. There is no evidence currently that lipid lowering therapy is unsafe in patients with COVID-19 infection. Lipid-lowering therapy should not be interrupted because of the pandemic or in patients at increased risk of COVID-19 infection. In patients with confirmed COVID-19, care should be taken to avoid drug interactions, between lipid-lowering medications and drugs that may be used to treat COVID-19, especially in patients with abnormalities in liver function tests.

[15] *Guo J, Li M, Yang Y et al.* **Pretreatment with atorvastatin ameliorates cobra venom factor-induced acute lung inflammation in mice**. BMC Pulm Med 2020; 20:263.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33046059

ABSTRACT

BACKGROUND: The complement system plays a critical role as the pathogenic factor in the models of acute lung injury due to various causes. Cobra venom factor (CVF) is a commonly used complement research tool. The CVF can cause acute inflammation in the lung by producing complement activation components. Atorvastatin (ATR) is a 3-hydroxy-3-methylglutaryl coenzyme A inhibitor approved for control of plasma cholesterol levels. This inhibitor can reduce the acute pulmonary inflammatory response. However, the ability of ATR in treating acute lung inflammation caused by complement activation is still unknown. Therefore, we investigated the effect of ATR on lung inflammation in mice induced by activation of the complement alternative pathway in this study. METHODS: ATR (10 mg/kg/day via oral gavage) was administered for 7 days before tail vein injection of CVF (25 μg/kg). On the seventh day, all mice were sacrificed 1 h after injection. The lung lobe, bronchoalveolar lavage fluid (BALF), and blood samples were collected. The myeloperoxidase (MPO) activity of the lung homogenate, the leukocyte cell count, and the protein content of BALF were measured. The levels of interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), P-selectin, and Intercellular cell adhesion molecule-1 (ICAM-1) in BALF and serum were determined by enzyme-linked immunosorbent assay. The pathological change of the lung tissue was observed by hematoxylin and eosin staining. The deposition of C5b-9 in the lung tissue was detected by immunohistochemistry. The phosphorylation of NF-κB p65 in the lung tissues was examined by immunohistochemistry and western blotting. RESULTS: The lung inflammation levels were determined by measuring the leukocyte cell numbers and protein content of BALF, the lung MPO activity, and expression and staining of the inflammatory mediators (IL-6 and TNF-α), and adhesion molecules (P-selectin and ICAM-1) for lung lesion. A significant reduction in the lung inflammation levels was observed after 7 days in ATR pre-treated mice with a CVF-induced lung disease. Deposition of C5b-9 was significantly alleviated by ATR pretreatment. Early intervention with ATR significantly reduced the development of acute lung inflammation on the basis of phosphorylation of NF-κB p65 in the lung. CONCLUSION: These findings suggest the identification of ATR treatment for the lung inflammation induced by activating the complement system on the basis of its anti-inflammatory response. Together with the model replicating the complement activating characteristics of acute lung injury, the results may be translatable to the overactivated complement relevant diseases.

[16] *Fisk HL, Kindberg GM, Hustvedt SO, Calder PC*. **A novel omega-3 glyceride mixture enhances enrichment of eicosapentaenoic acid and docosahexaenoic acid after single**

dosing in healthy older adults: results from a double-blind crossover trial. The British journal of nutrition 2020:1-19.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33046141
ABSTRACT
A glyceride mix of mono, di, and triglycerides increases solubilisation and enhances emulsification of omega-3 (ω-3) fatty acid (FA) containing lipids in the stomach. This allows for better access of digestive enzymes, pivotal for the release of bioactive ω-3 FA.The objective was to compare the effect of a glyceride formulation and an ethyl ester (EE) formulation of EPA+DHA on concentrations of EPA and DHA in plasma following single dosing.We conducted a double-blind crossover trial in which twenty healthy adults aged 50-70 y consumed a single dose (2.8 g EPA+DHA) of each EPA+DHA formulation without a meal in random order separated by a two-week wash out period. EPA and DHA were measured in plasma total lipid over the following 12 h.EPA and DHA in plasma total lipid increased over 12 h with both formulations. A 10 x greater Δ concentration of EPA, 3 x greater Δ concentration of DHA, and 5 x greater Δ concentration of EPA+DHA was seen with the glyceride-EPA+DHA. The time at which the maximal concentrations of ω-3 FA occurred was 4 h earlier for EPA, 1 h earlier for DHA, and 2 h earlier for EPA+DHA when consuming glyceride-EPA+DHA.A mix of mono, di, and triglycerides results in greater and faster incorporation of EPA and DHA into blood plasma lipid in the absence of a fatty meal. This may provide benefit to individuals on a low fat diet or with digestive impairments and could result in greater efficacy in clinical trials using ω-3 FA.

[17] *Dutheil F, Baker JS, Mermillod M et al.* **Shift work, and particularly permanent night shifts, promote dyslipidaemia: A systematic review and meta-analysis**. Atherosclerosis 2020; 313:156-169.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33069952
ABSTRACT
BACKGROUND AND AIMS: Shift work is common worldwide and linked to deleterious cardiovascular effects that might be underlined by dyslipidemia. The aim of this systematic review and meta-analysis is to determine the impact of shiftwork on dyslipidemia. METHODS: Searching in PubMed, Cochrane Library, Science Direct and Embase databases without language restriction on 15 February 2020, included studies that describe blood lipids levels or a risk measure in shift workers compared with fixed-day workers (controls). Differences by study-level characteristics were estimated using stratified meta-analysis by type of shift work, and meta-regression to examine relations between dyslipidemia and demographic, lifestyle and work characteristics. Estimates were pooled using random-effect meta-analysis. RESULTS: We included a total of 66 articles, representing 197,063 workers. Shift work globally increased the levels of triglycerides (overall SMD = 0.09; 95CI 0.05 to 0.13; p < 0.001), and globally decreased the levels of c-HDL (-0.08; 95CI -0.12 to -0.03; p = 0.001). Permanent night shift workers were an at-risk type of shift for dyslipidemia with significantly higher blood levels of total cholesterol (0.22; 95CI 0.01 to 0.42; p = 0.043) and triglycerides (0.18; 0.03 to 0.33; p = 0.017), and significantly lower blood levels of c-HDL (-0.16; 95CI -0.32 to 0.00; p = 0.05). Permanent night shift workers were more at-risk for total cholesterol than rotating 3 × 8 shift workers (Coefficient 0.22; 95CI 0.01 to 0.42; p = 0.038) and rotating 2 × 12 shift workers (0.24; 0.02 to 0.46; p = 0.037), and more at-risk for triglycerides than rotating day shift workers (0.21; 95CI 0.03 to 0.38; p = 0.023). Results were non-significant for c-LDL, nor

depending on type of shifts. CONCLUSIONS: Shift work, and particularly permanent night shift, is associated with dyslipidaemia via elevated total cholesterol and triglycerides, and reduced HDL-cholesterol. Our current study provides a practical and valuable strengthening of the evidence-base required for preventive health initiatives and workplace reform.

[18] *Basalay MV, Yellon DM, Davidson SM*. **Targeting myocardial ischaemic injury in the absence of reperfusion**. Basic research in cardiology 2020; 115:63.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33057804
ABSTRACT
Sudden myocardial ischaemia causes an acute coronary syndrome. In the case of ST-elevation myocardial infarction (STEMI), this is usually caused by the acute rupture of atherosclerotic plaque and obstruction of a coronary artery. Timely restoration of blood flow can reduce infarct size, but ischaemic regions of myocardium remain in up to two-thirds of patients due to microvascular obstruction (MVO). Experimentally, cardioprotective strategies can limit infarct size, but these are primarily intended to target reperfusion injury. Here, we address the question of whether it is possible to specifically prevent ischaemic injury, for example in models of chronic coronary artery occlusion. Two main types of intervention are identified: those that preserve ATP levels by reducing myocardial oxygen consumption, (e.g. hypothermia; cardiac unloading; a reduction in heart rate or contractility; or ischaemic preconditioning), and those that increase myocardial oxygen/blood supply (e.g. collateral vessel dilation). An important consideration in these studies is the method used to assess infarct size, which is not straightforward in the absence of reperfusion. After several hours, most of the ischaemic area is likely to become infarcted, unless it is supplied by pre-formed collateral vessels. Therefore, therapies that stimulate the formation of new collaterals can potentially limit injury during subsequent exposure to ischaemia. After a prolonged period of ischaemia, the heart undergoes a remodelling process. Interventions, such as those targeting inflammation, may prevent adverse remodelling. Finally, harnessing of the endogenous process of myocardial regeneration has the potential to restore cardiomyocytes lost during infarction.

[19] *Wang H, Li Y, Zhang X et al.* **DPP-4 Inhibitor Linagliptin Ameliorates Oxidized LDL-Induced THP-1 Macrophage Foam Cell Formation and Inflammation**. Drug design, development and therapy 2020; 14:3929-3940.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33061298
ABSTRACT
INTRODUCTION: Atherosclerosis is one of the major causes of cardiovascular diseases. Lipid uptake and accumulation in macrophages play a major role in atherosclerotic plaque formation from its initiation to advanced atheroma formation. The dipeptidyl peptidase-4 (DPP-4) inhibitor Linagliptin is commonly used to lower blood glucose in type 2 diabetes patients. Recent studies report that Linagliptin has cardiovascular protective and anti-inflammatory effects. METHODS: THP-1 macrophage cells were treated with 100 nM PMA for 72 hour to induce foam cell formation. The differentiated cells were exposed to 100 μg/mL ox-LDL in the presence or absence of the DPP-4 inhibitor Linagliptin. The expression levels of DPP-4 and inflammatory cytokines were detected by RT-PCR, ELISA, and Western blot experiments. The cellular ROS level was measured by staining the cells with the fluorescent probe DCFH-DA. The separation of lipoprotein fractions was achieved by high-performance liquid

chromatography (HPLC). The cells were labeled with fluorescent-labeled cholesterol to measure cholesterol efflux, and lipid droplets were revealed by Nile red staining. RESULTS: The presence of Linagliptin significantly reduced ox-LDL-induced cytokine production (IL-1β and IL-6) and ROS production. Linagliptin ameliorated ox-LDL-induced lipid accumulation and impaired cholesterol efflux in macrophages. Mechanistically, this study showed that Linagliptin mitigated ox-LDL-induced expression of the scavenger receptors CD36 and LOX-1, but not SRA. Furthermore, Linagliptin increased the expression of the cholesterol transporter ABCG1, but not ABCA1. CONCLUSION: Linagliptin possesses a potent inhibitory effect on THP-1 macrophage-derived foam cell formation in response to ox-LDL. This effect could be mediated through a decrease in the expression of CD36 and LOX-1 on macrophages and an increase in the expression of the cholesterol transporter ABCG1. This study indicates that the DPP-4 inhibitor Linagliptin plays a critical role in preventing foam cell formation in vitro. However, future research using an atherosclerotic animal model is necessary to determine its effectiveness and to prove its potential implication in the prevention and treatment of atherosclerosis.

[20] *Toorang F, Sasanfar B, Esmaillzadeh A et al.* **Comparison of validity of the Food Frequency Questionnaire and the Diet History Questionnaire for assessment of energy and nutrients intakes in an Iranian population**. East Mediterr Health J 2020; 26:1062-1069.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33047797
ABSTRACT
BACKGROUND: Dietary intakes are important for development and prevention of chronic disease. The Food Frequency Questionnaire (FFQ) has been suggested as an acceptable feasible method for assessing the association of dietary intake and disease. However, FFQs are sensitive to dietary habits and culture and should be valid in the study population. AIMS: We investigated the validity of the Diet History Questionnaire (DHQ) and the Food Frequency Questionnaire in healthy Iranians. METHODS: Participants were healthy relatives of cancer patients in the Cancer Institute of Iran. They participated in face-to-face interviews. We took telephone based 24-hour recalls every 2 months over a 1-year period. Assuming the mean intakes of 24-hour recalls as the gold standard, we estimated Pearson correlation coefficients to measure the reliability of the FFQ and the DHQ. We investigated how the FFQ or DHQ categorized individuals in different intake groups comparing with the 24-hour recalls. RESULTS: Overall, 102 subjects took part in our study. Deattenuated Spearman correlations were ≥ 0.5 for energy, carbohydrate, protein, carotene, niacin, folate, vitamin B(12), biotin, vitamin C, iron, zinc and selenium in both DHQ and FFQ. Level of agreement with 24-hour recall in classifying individuals into different categories of intakes ranged from 0.81 for riboflavin and carotene to 0.92 for carbohydrate and zinc in the DHQ and from 0.75 for riboflavin to 0.96 for carbohydrate in the FFQ. CONCLUSIONS: Both DHQ and FFQ were valid in assessing most nutrient intakes and classifying individuals in different categories of intakes in the Iranian population.

[21] *Sfikas G, Psallas M, Koumaras C et al.* **Prevalence, diagnosis and treatment with 3 different statins of non-alcoholic fatty liver disease/non-alcoholic steatohepatitis in military personnel. Do genetics play a role?** Current vascular pharmacology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33059580
ABSTRACT

BACKGROUND: Non-alcoholic fatty liver disease (NAFLD) and its severe form, non-alcoholic steatohepatitis (NASH), are major health problems worldwide. Genetics may play a role in the pathogenesis of NAFLD/NASH. AIM: To investigate the prevalence of NAFLD/NASH in 5,400 military personnel and evaluate the effect of treatment with 3 statins on NAFLD/NASH using 2 non-invasive scores [NAFLD Activity Score (NAS); Fibrosis-4 score (FIB-4)]. METHODS: During the mandatory annual medical check-up, military personnel underwent a clinical and laboratory evaluation. Participants with NAFLD/NASH were randomised to 4 groups (n=151 each): dietexercise, atorvastatin, rosuvastatin or pitavastatin for 1 year (i.e. until the next routine evaluation). RESULTS: From all the participants, 613 had NAFLD/NASH (prevalence 11.3 vs 39.8% in the general population, p<0.001); 604 consented to participate in the study. After a year of treatment, the diet-exercise group showed no significant changes in both scores (NAS 4.98 baseline vs 5.62, p=0.07; FIB-4 3.42 vs 3.52, p=0.7). For the atorvastatin group, both scores were reduced (NAS 4.97 vs 1.95, p<0.001, FIB-4 3.56 vs 0.83, p<0.001), for rosuvastatin (NAS 5.55 vs 1.81, p<0.001, FIB-4 3.61 vs 0.79, p<0.001), and for pitavastatin (NAS 4.89 vs 1.99, p<0.001, FIB-4 3.78 vs 0.87, p<0.001). CONCLUSIONS: Atorvastatin, rosuvastatin and pitavastatin have a beneficial and safe effect in NAFLD/NASH patients as recorded by the improvement in the NAS (representing NAFLD activity) and FIB-4 (representing liver fibrosis) scores. Since both those with and without NAFLD/NASH shared several baseline characteristics, genetics may play a role in the pathogenesis of NAFLD/NASH and its treatment with statins.

[22] *Roa Garrido J, Carrasco Salas P, Toscano Pérez C et al.* **Genetics and biochemistry of familial hypercholesterolemia in Southwest of the Iberian Peninsula**. Clinica e investigacion en arteriosclerosis : publicacion oficial de la Sociedad Espanola de Arteriosclerosis 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33069457
ABSTRACT
So far, most cases of hypercholesterolaemia (60-80%) are attributed to pathogenic variants in the LDLR gene. Only 1-5% of cases are caused by variants in the APOB gene, and 0-3% by variants in the PCSK9 gene. There is a large variety in known pathogenic mutations of the LDLR gene, while for those affecting the APOB gene, the highest incidence is p.Arg3527Gln, described predominantly in Central European and North American populations. In the Iberian Peninsula the predominant gene affected is that of the LDL receptor, similar to the rest of the world, with the involvement of the APOB gene being described in individuals from the northwest, and anecdotal in the rest of the territory. A genetics analysis was performed on the population attending the first year of a lipid clinic in southwestern Spain with a 6-point score from the Dutch lipid clinics. The genetic, biochemical and clinical findings are described. The first findings show indications of a possible higher prevalence of patients with mutation in the APOB gene compared to other territories. Historical evidence is presented that could give a possible explanation to this, thus supporting the assumption.

[23] *Rakipovski G, Hovingh GK, Nyberg M*. **Proprotein convertase subtilisin/kexin type 9 inhibition as the next statin?** Current opinion in lipidology 2020; 31:340-346.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33060383
ABSTRACT

PURPOSE OF REVIEW: Despite the wide use of statins and other LDL-cholesterol (LDL-C)-lowering therapies, atherosclerotic cardiovascular disease remains an important cause of mortality and morbidity. Here, we discuss efficacy, side effects and convenience of current and future therapies inhibiting proprotein convertase subtilisin/kexin type 9 (PCSK9). RECENT FINDINGS: Clinical trials with mAbs administered every 2-4 weeks and small interfering RNAs given two to four times per year have consistently demonstrated substantial LDL-C-lowering (40-60%) and improved outcome when added to existing lipid-lowering therapies. Pleiotropic effects of PCSK9 inhibition are somewhat different from those observed with statin treatment as evidenced by reduced levels of triglycerides and lipoprotein(a) with no apparent effect on inflammatory markers in patients treated with PCSK9 inhibitors. Treatment with mAb and small interfering RNA are associated with a high-cost, however, small molecules and vaccines may improve cost and convenience if development of these are successful. SUMMARY: PCSK9 inhibitors are currently considered to be an add-on therapy and whether these drugs will be used as stand-alone and/or as a first choice is dependent on clinical readouts from ongoing and future trials, real-world evidence, convenience and treatment costs.

[24] *Naresh S, Bitla AR, Rao P et al.* **Correction to: Efficacy of oral rosuvastatin intervention on HDL and its associated proteins in men with type 2 diabetes mellitus**. Endocrine 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33048276
ABSTRACT
An amendment to this paper has been published and can be accessed via a link at the top of the paper.

[25] *Luo R, Sun X, Shen F et al.* **Effects of High-Dose Rosuvastatin on Ventricular Remodelling and Cardiac Function in ST-Segment Elevation Myocardial Infarction**. Drug design, development and therapy 2020; 14:3891-3898.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33061295
ABSTRACT
OBJECTIVE: To investigate the effects of high-dose rosuvastatin on ventricular remodelling and cardiac function in ST-segment elevation myocardial infarction (STEMI). MATERIALS AND METHODS: From January 2017 to March 2019, the clinical data of 93 patients with STEMI were collected and analysed, with 46 cases in the conventional-dose group (rosuvastatin, 10 mg/d) and 47 cases in the high-dose group (rosuvastatin, 20 mg/d). Blood lipid (TC, TG, LDL-C and HDL-C), serum inflammatory markers (hs-CRP, IL-6, TNF-α and ICAM-1), ventricular remodelling markers (NT-pro BNP, MMP-9, TIMP-4 and Gal-3) and indicators of cardiac function (LVESD, LVESD, LVESV, LVEDV, IVST and LVEF) were collected from all patients at the time of admission and 8 weeks after rosuvastatin treatment. RESULTS: After treatment with rosuvastatin for 8 weeks, compared with those in conventional-dose group, the levels of TC, TG, LDL-C, hs-CRP, IL-6, TNF-α, ICAM-1, NT-pro BNP, MMP-9 and Gal-3 in the high-dose group decreased significantly ($P<0.05$), while the increase of HDL-C and TIMP-4 levels was more obvious ($P<0.05$) than that in the conventional-dose group. Moreover, LVEF was significantly higher ($P<0.05$) and LVESD, LVESD, LVESV, LVEDV and IVST were significantly lower ($P< 0.05$) after treatment than before treatment in both groups. The improvement of cardiac ultrasound results in the high-dose group was more significant than that in the conventional-dose group ($P< 0.05$). CONCLUSION: This study suggests that

high-dose rosuvastatin was better than conventional-dose rosuvastatin for improving blood lipid metabolism, reducing the inflammatory response, and preventing and treating ventricular remodelling and myocardial fibrosis, indicating that high-dose rosuvastatin had stronger therapeutic effect on STEMI than conventional-dose rosuvastatin.

[26] *Liu Z, Zhang F, Zhao L et al.* **Protective Effect of Pravastatin on Myocardial Ischemia Reperfusion Injury by Regulation of the miR-93/Nrf2/ARE Signal Pathway**. Drug design, development and therapy 2020; 14:3853-3864.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33061292
ABSTRACT
PURPOSE: This research intended to study the mechanism of pravastatin in myocardial ischemia reperfusion (I/R) injury. PATIENTS AND METHODS: Altogether 70 male rats were selected and grouped into Sham operation group (Sham group), ischemia reperfusion group (I/R group), pravastatin pretreatment group (I/R+P group), I/R+miR-93-mimics, I/R+P+miR-93-mimics, I/R+Nrf2 siRNA, and I/R+P+Nrf2 siRNA group. The myocardial function of each group was detected. RESULTS: Myocardial I/R injury could lead to abnormal myocardial enzyme activity, inflammatory reaction and oxidative stress. However, pravastatin could significantly inhibit the activity of myocardial enzymes, alleviate inflammatory reaction and inhibit oxidative stress reaction, thus playing a protective role. Furthermore, cell experiments showed that pravastatin can alleviate the injury of H9C2 myocardial cells caused by I/R, inhibit the apoptosis of myocardial cells, and lead to a significant reduction in pro-apoptotic genes Bax, caspase-3 and caspase-9 transcription levels, an obvious increase in anti-apoptotic gene Bcl-2, and an increase in cell activity. After I/R induced injury, miR-93 level was significantly up-regulated and Nrf2 level was down-regulated. Over-expression of miR-93 or inhibition of Nrf2 expression would lead to further aggravation of I/R myocardial injury, increase the apoptosis rate of cells and decrease the activity of myocardial cells. Pravastatin administration could inhibit miR-93, activate and promote Nrf2 in myocardial tissue, and promote protein expression of downstream regulatory genes HO-1 and NQO1. In the I/R model, pravastatin was given. Over-expression of miR-93 or silencing Nrf2 could reverse the therapeutic effect of pravastatin on I/R. CONCLUSION: Pravastatin acts as a protector on myocardial ischemia reperfusion injury by regulating miR-93/Nrf2/ARE signaling pathway.

[27] *Kumar V, Yin M, Ishida K et al.* **Prediction of Transporter-Mediated Rosuvastatin Hepatic Uptake Clearance and Drug Interaction in Humans Using Proteomics-Informed REF Approach**. Drug metabolism and disposition: the biological fate of chemicals 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33051248
ABSTRACT
Suspended (SH), plated (PH) or sandwich-cultured human hepatocytes (SCHH) are routinely used for in vitro to in vivo extrapolation (IVIVE) of transporter-mediated hepatic clearance (CL) of drugs. However, these hepatocyte models have been reported to underpredict transporter-mediated in vivo hepatic uptake CL (CL(uptake, in vivo)) of some drugs. Therefore, we determined if transporter-expressing cells (TEC) can accurately predict the CL(uptake, in vivo) of drugs. To do so, we determined the uptake CL (CL(int,uptake,cells)) of rosuvastatin (RSV) by TEC (OATPs/NTCP) and then scaled it to that in vivo by REF (the ratio of transporter abundance in human livers and TEC) determined by LC-MS/MS-based quantitative proteomics. Both the TEC and hepatocyte models did not meet our pre-defined success

criteria of predicting within 2-fold the RSV CL(uptake, in vivo) value obtained from our PET imaging. However, the TEC performed better than the hepatocyte models. Interestingly, using REF, TEC successfully predicted RSV CL(int,uptake,hep) obtained by the hepatocyte models, suggesting that the underprediction of RSV CL(uptake, in vivo) by TEC and hepatocytes is due to an endogenous factor(s) not present in these in vitro models. Therefore, we determined if inclusion of plasma (or albumin) in TEC uptake studies, improved IVIVE of RSV CL(uptake, in vivo) It did, but our predictions still fell shy of our pre-defined 2-fold lower boundary. Thus, additional studies are needed to improve transporter-mediated IVIVE of hepatic uptake CL of drugs. However, using REF and TEC, we successfully predicted the magnitude of PET-imaged inhibition of RSV CL(uptake, in vivo) by cyclosporine A. Significance Statement We showed that the in vivo transporter-mediated uptake CL of rosuvastatin, determined by PET imaging, cannot be accurately predicted from in vitro studies in transporter-expressing cells (scaled using REF) or human hepatocytes (scaled based on mg of protein per g of liver). This conclusion held irrespective of whether albumin or plasma was included in the in vitro studies. Thus, additional studies are needed to improve IVIVE of transporter-mediated drug CL.

[28] *El Missiri A, Amin SA, Tawfik IR, Shabana AM*. **Effect of a 6-week and 12-week cardiac rehabilitation program on heart rate recovery**. The Egyptian heart journal : (EHJ) : official bulletin of the Egyptian Society of Cardiology 2020; 72:69.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33052491

ABSTRACT

BACKGROUND: Cardiac rehabilitation has been shown to reduce cardiac mortality, improve quality of life, and reduce hospitalizations. Cardiac rehabilitation programs are usually performed over a 12-week period. Studies have shown that similar benefits could be achieved with shorter programs. Abnormal heart rate recovery after exercise has been associated with an increased risk of cardiovascular events and mortality. The main aim of this study was to compare the effect of a 6-week phase 2 cardiac rehabilitation program on heart rate recovery to a 12-week one in patients who had recovered from an anterior wall ST segment elevation myocardial infarction. RESULTS: This prospective study included 60 patients enrolled in cardiac rehabilitation programs randomized into two equal groups: a 6-week and a 12-week program. Baseline patient demographics, lipid profile, and left ventricular ejection fraction (LVEF) were assessed. METs achieved, total exercise time, resting heart rate, peak heart rate, and heart rate recovery at 1 min were examined. These were re-assessed at the end of each program. Results showed no difference between both groups at the end of each program regarding lipid profile and LVEF. Patients enrolled in the 12-week cardiac rehabilitation program were able to achieve more METs, had a longer exercise time, a higher peak heart rate, and had a lower resting heart rate at the end of the program. Heart rate recovery was slightly higher in patients enrolled in the 6-week program 26.5 ± 6.78 versus 23.17 ± 6.12 bpm ($p = 0.051$). On comparing the magnitude of change between both programs, those in the 12-week program had more increase in HDL-C levels, METs achieved, and exercise time. Additionally, they had more reduction of resting heart rate. Heart rate recovery was more increased for those in the 6-week program. CONCLUSION: Although heart rate recovery increases after completion of each of a 6-week and 12-week cardiac rehabilitation program compared to their baseline, there is no difference on comparing heart rate recovery between both programs at their end. Patients enrolled in a standard 12-week cardiac rehabilitation

program achieve more METs, have a longer exercise time, a higher peak HR, and a lower resting HR at the end of the program compared to those in the 6-week program.

[29] *Carter P, Vithayathil M, Kar S et al.* **Predicting the effect of statins on cancer risk using genetic variants from a Mendelian randomization study in the UK Biobank**. eLife 2020; 9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33046214
ABSTRACT
Laboratory studies have suggested oncogenic roles of lipids, as well as anticarcinogenic effects of statins. Here we assess the potential effect of statin therapy on cancer risk using evidence from human genetics. We obtained associations of lipid-related genetic variants with the risk of overall and 22 site-specific cancers for 367,703 individuals in the UK Biobank. In total, 75,037 individuals had a cancer event. Variants in the HMGCR gene region, which represent proxies for statin treatment, were associated with overall cancer risk (odds ratio [OR] per one standard deviation decrease in low-density lipoprotein [LDL] cholesterol 0.76, 95% confidence interval [CI] 0.65-0.88, p=0.0003) but variants in gene regions representing alternative lipid-lowering treatment targets (PCSK9, LDLR, NPC1L1, APOC3, LPL) were not. Genetically predicted LDL-cholesterol was not associated with overall cancer risk (OR per standard deviation increase 1.01, 95% CI 0.98-1.05, p=0.50). Our results predict that statins reduce cancer risk but other lipid-lowering treatments do not. This suggests that statins reduce cancer risk through a cholesterol independent pathway.

[30] *Pizano-Zárate ML, Horta-Baas G, Nuñez-Hernández JA et al.* **Prevalence and characteristics of the metabolically healthy obese phenotype in children and adolescents in a Mexican state**. Endocrinologia, diabetes y nutricion 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33051160
ABSTRACT
OBJECTIVES: To determine the prevalence of the Metabolically Healthy Obesity (MHO), and Metabolically Obese Normal-Weight (MONW) phenotypes in a sample of children and adolescents. To evaluate which clinical and laboratory variables are related to the MONW and MHO phenotypes. METHODS: A cross-sectional study was carried out in children and adolescents aged 6-18 years old, presumably healthy. Somatometry, glucose, insulin, triglycerides, HDL-cholesterol, LDL-cholesterol, HOMA-IR, triglycerides/HDL ratio, triglycerides and glucose index, and leptin/adiponectin, were determined. RESULTS: Data from 620 children and adolescents were included (50.65% were males); the median age was 11 years. The prevalence of the MONW phenotype was 22.85% (95%CI 16.85%-29.79%), and the MHO phenotype 27.61% (95%CI 22.60%-33.06%). The variables that significantly explained the possibility of presenting the MONW and MHO phenotype were triglycerides/HDL ratio, and product of triglycerides and glucose. Insulin and HOMA-IR were significantly associated with the MHO phenotype but not with the MONW phenotype. CONCLUSIONS: Prevalence of metabolically healthy obese phenotype is lower in the Mexican population compared to European studies; thus, future studies should determine if this difference relies upon genetic profile or lifestyle. The indices to assess the action of insulin based on lipids can help identify children and adolescents with the MHO and MONW phenotypes.

[31] *Parhofer KG, Chapman MJ, Nordestgaard BG*. **Efficacy and safety of icosapent ethyl in hypertriglyceridaemia: a recap**. European heart journal supplements : journal of the European Society of Cardiology 2020; 22:J21-j33.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33061865
ABSTRACT
Although low-density lipoprotein cholesterol lowering is effective in atherosclerotic cardiovascular disease (ASCVD) prevention, considerable 'lipid-associated' residual risk remains, particularly in patients with mild-to-moderate hypertriglyceridaemia (2-10 mmol/L; 176-880 mg/dL). Triglyceride (TG)-rich lipoproteins carry both TGs and cholesterol (remnant-cholesterol). At TG levels >5 mmol/L (440 mg/dL) vs. <1 mmol/L (88 mg/dL) or remnant-cholesterol >2.3 mmol/L (89 mg/dL) vs. <0.5 mmol/L (19 mg/dL), risk is ∼1.5-fold elevated for aortic stenosis, 2-fold for all-cause mortality, 3-fold for ischaemic stroke, 5-fold for myocardial infarction (MI), and 10-fold for acute pancreatitis. Furthermore, Mendelian randomization studies indicate that elevated TG-rich lipoproteins are causally related to increased risk of ASCVD and even all-cause mortality. While genetic and epidemiological data strongly indicate that TG-rich lipoproteins are causally linked to ASCVD, intervention data are ambiguous. Fibrates, niacin and low-dose omega-3 fatty acids have all been used in outcome trials, but have failed to demonstrate clear benefit in combination with statins. Whether the lack of additional benefit relates to methodological issues or true failure is indeterminate. Importantly, a recent intervention trial evaluating a high dose of eicosapentaenoic-acid showed clear benefit. Thus, REDUCE-IT evaluated the effect of icosapent ethyl (4 g/day) on cardiovascular outcomes in 8179 high-risk patients with moderate TG elevation on statin therapy. Over a median duration of 4.9 years, the relative risk for the primary endpoint (composite of cardiovascular death, non-fatal MI, non-fatal stroke, coronary revascularization, or unstable angina) was reduced by 25% (absolute risk 17.2% vs. 22.0%; $P < 0.0001$; number needed to treat 21). High-dose icosapent ethyl intervention therefore confers substantial cardiovascular benefit in high-risk patients with moderate hypertriglyceridaemia on statin therapy.

[32] *Mrakic-Sposta S, Gussoni M, Dellanoce C et al.* **Effects of acute and sub-acute hypobaric hypoxia on oxidative stress: a field study in the Alps**. European journal of applied physiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33057877
ABSTRACT
PURPOSE: High altitude results in lower barometric pressure and hence partial pressure of O(2) decrease can lead to several molecular and cellular changes, such as generation of reactive oxygen species (ROS). Electron Paramagnetic Resonance technique was adopted in the field, to evaluate the effects of acute and sub-acute hypobaric hypoxia (HH) on ROS production by micro-invasive method. Biological biomarkers, indicators of oxidative stress, renal function and inflammation were investigated too. METHODS: Fourteen lowlander subjects (mean age 27.3 ± 5.9 years) were exposed to HH at 3269 m s.l. ROS production, related oxidative damage to cellular components, systemic inflammatory response and renal function were determined through blood and urine profile performed at 1st, 2nd, 4th, 7th, and 14th days during sojourn. RESULTS: Kinetics of changes during HH exposition showed out significant (range $p < 0.05$-0.0001) increases that at max corresponds to 38% for ROS production rate, 140% for protein carbonyl, 44% for lipid peroxidation, 42% for DNA damage, 200% for inflammatory cytokines and modifications in renal function (assessed by neopterin

concentration: 48%). Conversely, antioxidant capacity significantly ($p < 0.0001$) decreased - 17% at max. CONCLUSION: This 14 days in-field study describes changes of oxidative-stress biomarkers during HH exposure in lowlanders. The results show an overproduction of ROS and consequent oxidative damage to protein, lipids and DNA with a decrease in antioxidant capacity and the involvement of inflammatory status and a transient renal dysfunction. Exposure at high altitude induces a hypoxic condition during acute and sub-acute phases accompanied by molecular adaptation mechanism indicating acclimatization.

[33] *Liu M, Fan F, Zhang Y, Li J*. **The association of GATM polymorphism with statin-induced myopathy: a systematic review and meta-analysis**. Eur J Clin Pharmacol 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33051696
ABSTRACT
PURPOSE: Statin-induced myopathy (SIM) is the commonest reason for discontinuation of statin therapy. The aim of this present meta-analysis is to assess the relationship between glycine amidinotransferase gene (GATM) polymorphism and risk of SIM. METHODS: MEDLINE, EMBASE, Web of Science, and Cochrane Library databases were searched systematically for case-control studies investigating the relationship between GATM polymorphism and SIM. Retrieved articles were carefully reviewed and assessed according to the inclusion criteria. Associations were assessed in pooled data by calculating odds ratio with 95% confidence intervals. Subgroup analysis was performed according to comedications and severity of SIM. RESULTS: Six studies with 707 cases and 2321 controls were included in this meta-analysis. GATM rs9806699 G>A was associated with decreased risk of SIM (OR = 0.80, 95% CI 0.68-0.94, P = 0.006). This association remained significant in the subgroup with fibrates or niacin excluded. However, the association of rs9806699 G>A with severe SIM was not significant. In addition, another two variations at GATM, rs1719247 C>T, and rs1346268 T>C were also associated with declined risk of SIM. CONCLUSIONS: GATM polymorphism including rs9806699 G>A, rs1719247 C>T, and rs1346268 T>C may be protective factors of SIM. GATM rs9806699 G>A may only exert protective effect on mild SIM cases. Our meta-analysis indicates that GATM polymorphism may represent a pharmacogenomics biomarker for predicting incidence of SIM, which contributes to risk stratification and optimizing statin adherence.

[34] *Landmesser U, Lindgren P, Hagström E et al.* **Cost-effectiveness of PCSK9 inhibition with evolocumab in patients with a history of myocardial infarction in Sweden**. European heart journal. Quality of care & clinical outcomes 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33063111
ABSTRACT
AIMS: To assess the cost-effectiveness of PCSK9 inhibition with evolocumab added to standard-of-care lipid-lowering treatment (maximum tolerated dose [MTD] of statin and ezetimibe) in Swedish patients with a history of myocardial infarction (MI). METHODS AND RESULTS: Cost-effectiveness was evaluated using a Markov model based on Swedish observational data on cardiovascular event rates and efficacy from the FOURIER trial. Three risk profiles were considered: recent MI in the previous year; history of MI with a risk factor; and history of MI with a second event within 2 years. For each population, three minimum baseline low-density lipoprotein cholesterol (LDL-C) levels were considered: 2.5 mmol/L (≈100 mg/dL), based on the current reimbursement recommendation in Sweden); 1.8 mmol/L

(≈70 mg/dL), based on 2016 ESC/EAS guidelines; and 1.4 mmol/L (≈55 mg/dL), or 1.0 mmol/L (≈40 mg/dL) for MI with a second event, based on 2019 ESC/EAS guidelines. PCSK9 inhibition with evolocumab was associated with increased quality-adjusted life-years and costs versus standard-of-care therapy. Incremental cost-effectiveness ratios (ICERs) were below SEK700,000 (~€66,500), the generally accepted willingness-to-pay threshold in Sweden, for minimum LDL-C levels of 2.3 (recent MI), 1.7 (MI with a risk factor) and 1.7 mmol/L (MI with a second event). Sensitivity analyses demonstrated that base-case results were robust to changes in model parameters. CONCLUSION: PCSK9 inhibition with evolocumab added to MTD of statin and ezetimibe may be considered cost-effective at its list price for minimum LDL-C levels of 1.7-2.3 mmol/L, depending on risk profile, with ICERs below the accepted willingness-to-pay threshold in Sweden.

[35] *Kasparian K, Graykowski D, Cudaback E*. **Commentary: APOE e4 Genotype Predicts Severe COVID-19 in the UK Biobank Community Cohort**. Frontiers in immunology 2020; 11:1939.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33042114
ABSTRACT

[36] *Heydarpour F, Sajadimajd S, Mirzarazi E et al.* **Involvement of TGF-β and Autophagy Pathways in Pathogenesis of Diabetes: A Comprehensive Review on Biological and Pharmacological Insights**. Frontiers in pharmacology 2020; 11:498758.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33041786
ABSTRACT
Despite recent advancements in clinical drugs, diabetes treatment still needs further progress. As such, ongoing research has attempted to determine the precise molecular mechanisms of the disorder. Specifically, evidence supports that several signaling pathways play pivotal roles in the development of diabetes. However, the exact molecular mechanisms of diabetes still need to be explored. This study examines exciting new hallmarks for the strict involvement of autophagy and TGF-β signaling pathways in the pathogenesis of diabetes and the design of novel therapeutic strategies. Dysregulated autophagy in pancreatic β cells due to hyperglycemia, oxidative stress, and inflammation is associated with diabetes and accompanied by dysregulated autophagy in insulin target tissues and the progression of diabetic complications. Consequently, several therapeutic agents such as adiponectin, ezetimibe, GABA tea, geniposide, liraglutide, guava extract, and vitamin D were shown to inhibit diabetes and its complications through modulation of the autophagy pathway. Another pathway, TGF-β signaling pathway, appears to play a part in the progression of diabetes, insulin resistance, and autoimmunity in both type 1 and 2 diabetes and complications in diabetes. Subsequently, drugs that target TGF-β signaling, especially naturally derived ones such as resveratrol, puerarin, curcumin, hesperidin, and silymarin, as well as Propolis, Lycopus lucidus, and Momordica charantia extracts, may become promising alternatives to current drugs in diabetes treatment. This review provides keen insights into novel therapeutic strategies for the medical care of diabetes.

[37] *Clark Iii D, Puri R, Nissen SE*. **Coronary Atherosclerotic Plaque Progression: Contributing Factors in Statin-Treated Patients**. Expert review of cardiovascular therapy 2020.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33048622

ABSTRACT

INTRODUCTION: Coronary atheroma progression correlates with adverse cardiovascular events among individuals with coronary artery disease. Atherosclerosis imaging, including coronary intravascular ultrasound (IVUS), has provided novel insights into the biologic contributors to atheroma progression or regression, improving the efficiency of drug development by identifying therapies most likely to succeed in clinical outcomes trials. AREAS COVERED: Despite widespread use of statins, residual risk for adverse events is high among individuals with cardiovascular disease receiving optimal medical therapy. This review outlines current studies, including patient-level analyses of large randomized clinical trials, demonstrating several factors that associate with coronary plaque progression in the context of statin therapies. EXPERT OPINION: Atherosclerotic plaque remains a fundamental substrate underlying the occurrence of ischemic events in the current era of cardiovascular care. Understanding pathobiologic contributors to atherosclerosis, targeting treatment pathways, generating high-quality data, and implementing evidence into clinical practice are necessary to improve outcomes among patients with atherosclerotic disease.

[38] *Cao R, Fang Z, Li S et al.* **Circulating Ceramide: A New Cardiometabolic Biomarker in Patients With Comorbid Acute Coronary Syndrome and Type 2 Diabetes Mellitus**. Front Physiol 2020; 11:1104.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33041846

ABSTRACT

AIMS: This study investigated the association of circulating ceramides in patients with comorbid acute coronary syndrome and type 2 diabetes mellitus (ACS-DM). METHODS: A total of 761 patients with coronary heart disease who were admitted to the Department of Cardiology at the Chinese PLA General Hospital from March to August 2018 were enrolled in this study. Of these 761 patients, 282 were diagnosed with acute coronary syndrome (ACS). We selected 65 patients with ACS-DM (ACS-DM group; mean age 64.88 years; 38 men) and 65 patients with ACS but without any comorbidities (ACS group; mean age 64.68 years; 38 men); the two groups were matched by age and sex. We determined four circulating ceramides in 130 plasma samples: Cer(d18:1/16:0), Cer(d18:1/18:0), Cer(d18:1/24:1), and Cer(d18:1/24:0). The ceramides in plasma samples from patients with ACS and those from patients with ACS-DM were compared. Pearson correlation coefficients between individual ceramides and traditional cardiovascular risk factors for the whole study population were calculated. Multiple logistic regression models were used to evaluate the relativity between the ceramide and ACS-DM. RESULTS: Compared with the ACS group, the levels of Cer(d18:1/16:0), Cer(d18:1/18:0), and Cer(d18:1/24:1) and their ratios to Cer(d18:1/24:0) were higher in the ACS-DM group and Cer(d18:1/24:0) was lower in the ACS-DM group ($P < 0.05$). Correlation analysis demonstrated mild-to-moderate correlations of ceramide and traditional cardiovascular risk factors. There were relatively strong correlations of Cer(d18:1/18:0) and Cer(d18:1/24:1) with C-reactive protein, blood lipids, fasting blood glucose, and glycated hemoglobin A(1)c. In multiple logistic regression models, Cer(d18:1/18:0) [odds ratio (OR) 2.396; 95% confidence interval (CI) 1.103-5.205; $P = 0.027$], Cer(d18:1/24:1) (OR 2.826; 95% CI 1.158-6.896; $P = 0.023$), Cer(d18:1/18:0)/Cer(d18:1/24:0) (OR 2.242; 95% CI 1.103-4.555; $P = 0.026$), and Cer(d18:1/24:1)/Cer(d18:1/24:0) (OR 2.673; 95% CI 1.225-5.836; $P = 0.014$) were positively correlated with ACS-DM, and Cer(d18:1/24:0) (OR 0.200; 95% CI 0.051-0.778;

P = 0.020) was negatively correlated with ACS-DM. CONCLUSION: Circulating ceramides are positively correlated with the risk of ACS-DM comorbidity. These results give a new insight into the pathogenesis of ACS-DM comorbidity and could provide new options for risk estimation.

[39] *Alkhalil M, Choudhury RP*. **Current concepts in atherosclerosis**. Indian J Thorac Cardiovasc Surg 2018; 34:198-205.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33060939
ABSTRACT
Atherosclerosis is a complex disease process. It is increasingly recognised that both lipoprotein retention and inflammatory cellular components are intricately related in the initiation and development of atherosclerotic plaque. LDL-c (cholesterol) has been long established as a cause for atherosclerosis; additionally, inflammatory cells such as monocytes and subsequently foam cells have also been directly linked to the progression of atherosclerotic disease. Emerging data suggest that structures outside vascular intima and media are also closely related to atherosclerosis. Perivascular adipose tissue (PVAT) may be a determinant of the inflammatory status of the atherosclerotic plaque. All these features are becoming extremely relevant as therapies against atherosclerosis are targeting both lipid retention and inflammation. Recently, there has been some success in these novel therapies, such as the proprotein convertase subtilisin-kexin type 9 (PCSK-9) inhibitor evolocumab and the interleukin-1ß neutralising antibody, canakinumab, in reducing cardiovascular events when added to standard therapy such as statin. This review will discuss the pathogenesis of atherosclerosis, including some novel features, and its management using new anti-atherosclerotic drugs.

[40] *Vitale M, Calabrese I, Massimino E et al.* **Dietary inflammatory index score, glucose control and cardiovascular risk factors profile in people with type 2 diabetes**. International journal of food sciences and nutrition 2020:1-8.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33045863
ABSTRACT
We examined the relationships between the dietary inflammatory index (DII(®)), dietary habits and cardiovascular risk factor profiles in people with type 2 diabetes mellitus (T2DM). Energy-adjusted DII (E-DII™) scores were calculated from a Food Frequency Questionnaire in 2568 T2DM patients from different parts of Italy. Analyses were conducted according to quartiles of sex-specific E-DII scores. Higher, more pro-inflammatory, (quartile 4) E-DII scores were associated with overall poor quality of the diet characterised by higher content of refined carbohydrates, added sugars, saturated fat and cholesterol and lower unsaturated fat, fibre and polyphenols compared to quartile 1. Higher E-DII scores also were associated with higher waist circumference (105.4 vs. 103.5 cm; p = 0.002), triglycerides (154.6 vs. 146.1 mg/dL; p = 0.005), diastolic blood pressure (80.05 vs. 78.6 mmHg; p = 0.04) and lower HDL-cholesterol (45.3 vs. 47.4 mg/dL; p = 0.04). In conclusion, E-DII is a potent marker of overall quality of the diet and is associated with an unfavourable cardiovascular risk factor profile.

[41] *Verhaart IEC, Cappellari O, Tanganyika-de Winter CL et al.* **Simvastatin Treatment Does Not Ameliorate Muscle Pathophysiology in a Mouse Model for Duchenne Muscular Dystrophy**. J Neuromuscul Dis 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33044191

ABSTRACT
Duchenne muscular dystrophy is an X-linked, recessive muscular dystrophy in which the absence of the dystrophin protein leads to fibrosis, inflammation and oxidative stress, resulting in loss of muscle tissue. Drug repurposing, i.e. using drugs already approved for other disorders, is attractive as it decreases development time. Recent studies suggested that simvastatin, a cholesterol lowering drug used for cardiovascular diseases, has beneficial effects on several parameters in mdx mice. To validate properly the effectiveness of simvastatin, two independent labs tested the effects of 12-week simvastatin treatment in either young (starting at 4 weeks of age) or adult (starting at 12 weeks of age) mdx mice. In neither study were benefits of simvastatin treatment observed on muscle function, histology or expression of genes involved in fibrosis, regeneration, oxidative stress and autophagy. Unexpectedly, although the treatment protocol was similar, simvastatin plasma levels were found be much lower than observed in a previous study. In conclusion, in two laboratories, simvastatin did not ameliorate disease pathology in mdx mice, which could either be due to the ineffectiveness of simvastatin itself or due to the low simvastatin plasma levels following oral administration via the food.

[42] *Stone GW, Maehara A, Ali ZA et al.* **Percutaneous Coronary Intervention for Vulnerable Coronary Atherosclerotic Plaque**. Journal of the American College of Cardiology 2020; 76:2289-2301.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33069847
ABSTRACT
BACKGROUND: Acute coronary syndromes most commonly arise from thrombosis of lipid-rich coronary atheromas that have large plaque burden despite angiographically appearing mild. OBJECTIVES: This study sought to examine the outcomes of percutaneous coronary intervention (PCI) of non-flow-limiting vulnerable plaques. METHODS: Three-vessel imaging was performed with a combination intravascular ultrasound (IVUS) and near-infrared spectroscopy (NIRS) catheter after successful PCI of all flow-limiting coronary lesions in 898 patients presenting with myocardial infarction (MI). Patients with an angiographically nonobstructive stenosis not intended for PCI but with IVUS plaque burden of ≥65% were randomized to treatment of the lesion with a bioresorbable vascular scaffold (BVS) plus guideline-directed medical therapy (GDMT) versus GDMT alone. The primary powered effectiveness endpoint was the IVUS-derived minimum lumen area (MLA) at protocol-driven 25-month follow-up. The primary (nonpowered) safety endpoint was randomized target lesion failure (cardiac death, target vessel-related MI, or clinically driven target lesion revascularization) at 24 months. The secondary (nonpowered) clinical effectiveness endpoint was randomized lesion-related major adverse cardiac events (cardiac death, MI, unstable angina, or progressive angina) at latest follow-up. RESULTS: A total of 182 patients were randomized (93 BVS, 89 GDMT alone) at 15 centers. The median angiographic diameter stenosis of the randomized lesions was 41.6%; by near-infrared spectroscopy-IVUS, the median plaque burden was 73.7%, the median MLA was 2.9 mm(2), and the median maximum lipid plaque content was 33.4%. Angiographic follow-up at 25 months was completed in 167 patients (91.8%), and the median clinical follow-up was 4.1 years. The follow-up MLA in BVS-treated lesions was 6.9 ± 2.6 mm(2) compared with 3.0 ± 1.0 mm(2) in GDMT alone-treated lesions (least square means difference: 3.9 mm(2); 95% confidence interval: 3.3 to 4.5; $p < 0.0001$). Target lesion failure at 24 months occurred in similar rates of BVS-treated and

GDMT alone-treated patients (4.3% vs. 4.5%; p = 0.96). Randomized lesion-related major adverse cardiac events occurred in 4.3% of BVS-treated patients versus 10.7% of GDMT alone-treated patients (odds ratio: 0.38; 95% confidence interval: 0.11 to 1.28; p = 0.12). CONCLUSIONS: PCI of angiographically mild lesions with large plaque burden was safe, substantially enlarged the follow-up MLA, and was associated with favorable long-term clinical outcomes, warranting the performance of an adequately powered randomized trial. (PROSPECT ABSORB [Providing Regional Observations to Study Predictors of Events in the Coronary Tree II Combined with a Randomized, Controlled, Intervention Trial]; NCT02171065).

[43] *Schiappacassa A, Maranhão PA, Souza M et al.* **Acute Effects of Metformin and Vildagliptin after a Lipid-Rich Meal on Postprandial Microvascular Reactivity in Patients with Type 2 Diabetes and Obesity: A Randomized Trial**. Journal of clinical medicine 2020; 9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33050169
ABSTRACT
BACKGROUND: Type 2 diabetes mellitus and obesity are both related to endothelial dysfunction. Postprandial lipemia is a cardiovascular risk. Notably, it is known that a high-fat diet may elicit microvascular dysfunction, even in healthy subjects. Since anti-diabetic drugs have different mechanisms of action and also distinct vascular benefits, we aimed to compare the results of two anti-diabetic drugs after the intake of a lipid-rich meal on microcirculation in patients with type 2 diabetes and obesity. In parallel, we also investigated the metabolic profile, oxidative stress, inflammation, plasma viscosity, and some gastrointestinal peptides. SUBJECTS/METHODS: We included 38 drug-naïve patients, all women aged between 19 and 50 years, with BMI ≥ 30 kg/m(2). We performed endothelial measurements and collected samples before (fasting) and after the intake of a lipid-rich meal at 30, 60, 120, and 180 min. Patients were randomized to metformin or vildagliptin, given orally just before the meal. Endothelial function was assessed by videocapillaroscopy and laser-Doppler flowmetry to investigate microvascular reactivity. Besides, we also investigated plasma viscosity, inflammatory and oxidative stress biomarkers, gastrointestinal peptides, and metabolic profile in all time points. RESULTS: No differences at baseline were noted between groups. Vildagliptin increased glucagon-like peptide-1 compared to metformin. Paired comparisons showed that, during the postprandial period, vildagliptin significantly changed levels of insulin and glucagon-like peptide-1, and also the dipeptidyl peptidase-4 activity, while metformin had effects on plasma glucose solely. Metformin use during the test meal promoted an increase in functional capillary density, while vildagliptin kept non-nutritive microvascular blood flow and vasomotion unchanged. CONCLUSIONS: After the intake of a lipid-rich meal, the use of vildagliptin preserved postprandial non-nutritive microflow and vasomotion, while metformin increased capillary recruitment, suggesting protective and different mechanisms of action on microcirculation.

[44] *Sah SK, Adhikary LP*. **Association Between Dyslipidemia and Serum Level of 25-Hydroxyvitamin-D in Early Chronic Kidney Disease, Not on Dialysis: An Observational Cross-Sectional Study from the Himalayan Country**. International journal of nephrology and renovascular disease 2020; 13:211-218.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33061530
ABSTRACT

BACKGROUND: Patients with CKD have a higher prevalence of dyslipidemia and hypovitaminosis than the normal population. Recent studies in the general population have shown a potential link between 25(OH)D and dyslipidemia. However, such evidence in the early CKD population, especially in the Nepalese setting, is lacking. Thus, the present study aimed at investigating the status of 25(OH)D and dyslipidemia in the early CKD patients, and further to establish an association between 25(OH)D and lipid profile. PATIENTS AND METHODS: In this cross-sectional study, we analyzed 136 clinically stable non-dialyzed CKD patients. 25(OH)D and lipid profile were evaluated as a core variable, and their direction and magnitude of a relationship were evaluated. RESULTS: The estimated prevalence of dyslipidemia was 49.3%, and 63.2% population had a deficiency of 25(OH)D level. Compared with the patient with normal 25(OH)D level, the patient with deficient 25(OH)D level had a significantly higher level of LDL-c (P=0.04) and lower level of HDL-C (P=0.048). Serum 25(OH)D level was significantly lower in dyslipidemic patients than non-dyslipidemic patients (P=0.015). Regression analysis demonstrated a significant inverse relationship between serum 25(OH)D levels and LDL-c (β=-1.5; P=<0.001), and TC levels (β=-1.4;P=0.003), and the association remained unchanged with further adjustment for age, sex, HTN, DM, serum albumin and eGFR. CONCLUSION: Our study unveiled a high rate of dyslipidemia and hypovitaminosis in a considerable number of early CKD patients. Low serum level of 25(OH)D was significantly correlated with a higher rate of dyslipidemia. These findings indicate some evidence for 25(OH)D level as a marker of dyslipidemia prediction, and that decrease in serum level of 25(OH)D is associated with increased serum level of LDL and TC; it could increase the risk of cardiovascular disease. Therefore, early recognition and timely management of hypovitaminosis and dyslipidemia is vital to prevent an inevitable cardiovascular event.

[45] *Mirzaei E, Mirjalili M, Jahangard L et al.* **Influence of Simvastatin as Augmentative Therapy in the Treatment of Generalized Anxiety Disorder: A Pilot Randomized, Placebo-Controlled Study**. Neuropsychobiology 2020:1-11.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33070132

ABSTRACT

BACKGROUND: Preliminary evidence is promising regarding the anxiolytic effects of statins in animal models of anxiety. Hence, this study aimed to evaluate the efficacy of simvastatin augmentation versus placebo in the treatment of patients with generalized anxiety disorder (GAD) with residual symptoms despite treatment with selective serotonin reuptake inhibitors (SSRIs). METHODS: A double-blind, 8-week controlled trial was conducted from August 2018 to December 2019 in an outpatient psychiatry clinic in Hamadan, Iran. A total of 138 patients with a diagnosis of GAD were assessed for eligibility. Of them, 84 patients who met the study criteria were randomly assigned either to the adjuvant simvastatin (20 mg/day) or to the placebo group. Standard medication consisting of SSRIs was consistent 2 months prior to and during the study. The severity of anxiety symptoms for each patient was assessed based on the Hamilton Anxiety Rating Scale (HAM-A) score at baseline, week 4, and week 8 after treatment. Additionally, blood lipid values were assessed at baseline and on completion of the study. RESULTS: Thirty-three out of 42 patients in the intervention group and 35 out of 42 patients in the control group completed the 8 weeks of the study period. Compared to the placebo group, in the simvastatin group cholesterol, triglycerides, and low-density lipoprotein significantly decreased, and high-density lipoprotein significantly increased over time. General linear model analysis demonstrated that although over time a higher decrease in mean HAM-A

scores was observed in the intervention group compared to the control group, this difference was not statistically significant (p = 0.11). In addition, at the end of the study, the number of responders and remitters was comparable in the two groups. CONCLUSIONS: The results from this clinical study did not support the potential efficacy of adjunctive simvastatin in the treatment of patients with GAD. Thus, large-scale and long-term clinical trials are required to more accurately assess the potential efficacy of statins in the treatment of patients with anxiety disorders.

[46] *Melin EO, Dereke J, Hillman M*. **Higher levels of the soluble receptor for advanced glycation end products and lower levels of the extracellular newly identified receptor for advanced glycation end products were associated with lipid-lowering drugs in patients with type 1 diabetes: a comparative cross-sectional study**. Lipids in health and disease 2020; 19:223.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33054750
ABSTRACT
BACKGROUND: The receptors for advanced glycation end products (RAGE) are increased in atherosclerotic plaques. Soluble (s)RAGE decreases, whereas the extracellular newly identified receptor for advanced glycation end products (EN-RAGE) increases inflammatory responses mediated by RAGE. The aims were to explore whether sRAGE, EN-RAGE and the EN-RAGE/sRAGE ratio, were associated with the use of lipid-lowering drugs (LLD) and/or antihypertensive drugs (AHD) in patients with type 1 diabetes (T1D). METHODS: Cross-sectional design. T1D patients were consecutively recruited from one diabetes clinic. Blood samples were collected, supplemented with data from electronic health records. sRAGE and EN-RAGE were analysed by enzyme linked immunosorbent assays. An EN-RAGE/sRAGE ratio was calculated. Adjustments were performed with inflammatory and metabolic variables, s-creatinine, depression, smoking, physical inactivity, medication, and cardiovascular complications. Multiple regression analyses were performed. RESULTS: In this study 283 T1D patients (men 56%, 18-59 years) were included. One-hundred and thirty LLD users compared to 153 non-users had lower levels of the EN-RAGE/sRAGE ratio (P = 0.009), and 89 AHD users compared to 194 non-users had lower levels of sRAGE (P = 0.031). The use of LLD (inversely) (B coefficient - 0.158, P = 0.033) and the use of AHD (B coefficient 0.187, P = 0.023) were associated with the EN-RAGE/sRAGE ratio. sRAGE (Lg10) (per unit) (adjusted odds ratio (AOR) = 3.5, 95% CI = 1.4-9.1, P = 0.009), EN-RAGE (Lg10) (per unit) (inversely) (AOR 0.4, 95% CI = 0.2-1.0, P = 0.046), age (P < 0.001), and triglycerides (P < 0.029), were associated with LLD. sRAGE (Lg10) (per unit) (inversely) (AOR = 0.2, 95% CI = 0.1-0.5, P = 0.001), diabetes duration, triglycerides, s-creatinine, and systolic BP (all P values < 0.043), were associated with AHD. CONCLUSIONS: Higher sRAGE levels and lower EN-RAGE levels were linked to the use of LLD, whereas lower sRAGE levels were linked to the use of AHD. No other variables but the use of LLD and the use of AHD were linked to the EN-RAGE/sRAGE ratio. This may be of major importance as sRAGE is an inhibitor and EN-RAGE is a stimulator of inflammatory processes mediated by RAGE.

[47] *Liu H, Xie G, Huang W et al.* **Rationale and design of a multicenter, randomized, patients-blinded two-stage clinical trial on effects of endothelial function test in patients with non-obstructive coronary artery disease (ENDOFIND)**. International journal of cardiology 2020.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33069784

ABSTRACT

Abnormal peripheral and coronary endothelial function has been associated with increased risk of major adverse cardiovascular events (MACE) in cross-sectional retrospective and observational studies. However, prognostic value of routine clinical evaluation, diagnosis and treatment of endothelial dysfunction on incident MACE in patients with non-obstructive coronary artery disease (NOCAD) remains unknown. Endothelial Function Guided Management in Patients with NOCAD (ENDOFIND) is a multicenter, randomized, patients-blinded, parallel-controlled, two-stage clinical trial evaluating the impact of routine clinical peripheral endothelial function testing on initiation and/or intensification of cardiovascular preventive therapies in Stage I, and on the risk of MACE in Stage II in patients with NOCAD. One thousand participants with NOCAD on clinically indicated coronary computed tomography or invasive angiography will be enrolled and randomized 1:1, after baseline peripheral endothelial function evaluation, to either endothelial function guided treatment group or standard of care control group. In Stage I, patients will be followed for 12 months and primary outcome will be the proportion of patients receiving prescriptions for cardiovascular evidence-based lipid, blood pressure and glucose lowering medications at the clinic visit immediately after endothelial function evaluation. Secondary outcomes are change in endothelial function measured as reactive hyperemia index and patients' adherence to evidence-based medications in 12 months. Study will be extended into Stage II where sample size and follow up duration will be reevaluated to ensure statistical power, and primary outcome will be incident MACE. ENDOFIND is proof-of-concept clinical trial of a disruptive endothelial function guided clinical intervention with potential benefits to NOCAD patients. CONDENSED ABSTRACT: ENDOFIND is a proof-of-concept clinical trial of a disruptive endothelial function guided clinical intervention with potential benefits to patients with no obstructive coronary artery disease (NOCAD). It is a multicenter, randomized, patients-blinded, parallel controlled two-stage clinical trial to evaluate the impact of routine clinical peripheral endothelial function testing on initiation and/or intensification of cardiovascular disease preventive therapies in Stage I, and on the risk of MACE in Stage II.

[48] *Kostyunin A, Mukhamadiyarov R, Glushkova T et al.* **Ultrastructural Pathology of Atherosclerosis, Calcific Aortic Valve Disease, and Bioprosthetic Heart Valve Degeneration: Commonalities and Differences**. International journal of molecular sciences 2020; 21.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33050133

ABSTRACT

Atherosclerosis, calcific aortic valve disease (CAVD), and bioprosthetic heart valve degeneration (alternatively termed structural valve deterioration, SVD) represent three diseases affecting distinct components of the circulatory system and their substitutes, yet sharing multiple risk factors and commonly leading to the extraskeletal calcification. Whereas the histopathology of the mentioned disorders is well-described, their ultrastructural pathology is largely obscure due to the lack of appropriate investigation techniques. Employing an original method for sample preparation and the electron microscopy visualisation of calcified cardiovascular tissues, here we revisited the ultrastructural features of lipid retention, macrophage infiltration, intraplaque/intraleaflet haemorrhage, and calcification which are common or unique for the indicated types of cardiovascular disease. Atherosclerotic plaques

were notable for the massive accumulation of lipids in the extracellular matrix (ECM), abundant macrophage content, and pronounced neovascularisation associated with blood leakage and calcium deposition. In contrast, CAVD and SVD generally did not require vasculo- or angiogenesis to occur, instead relying on fatigue-induced ECM degradation and the concurrent migration of immune cells. Unlike native tissues, bioprosthetic heart valves contained numerous specialised macrophages and were not capable of the regeneration that underscores ECM integrity as a pivotal factor for SVD prevention. While atherosclerosis, CAVD, and SVD show similar pathogenesis patterns, these disorders demonstrate considerable ultrastructural differences.

[49] *Grgurević D, Grgurević J, Bačić Vrca V et al.* **Consumption of high-dose statins in patients older than 65 years in the Republic of Croatia in the period 2005 - 2015**. International journal of clinical pharmacology and therapeutics 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33040840
ABSTRACT
OBJECTIVE: Patients over 65 years of age on high-dose statins are most sensitive to the development of adverse effects of statins. The objective of this study is to analyze the consumption of high-dose statins in this patient group in Croatia in the period of 2005 - 2015. MATERIALS AND METHODS: For the period of January 1, 2005 to December 31, 2015, the Croatian Institute for Health Insurance provided us with the total number of: all insured, insured over 65 years of age, insured using statins, insured using high-dose statins, insured over 65 using statins, insured over 65 using high-dose statins, number of packages dispensed through all community pharmacies for all statins registered in Croatia divided by year and sex. Studied high-dose statins were: simvastatin 40 mg; atorvastatin 40 mg, 60 mg, 80 mg; fluvastatin 80 mg; rosuvastatin 40 mg. The yearly consumption of each form of statin was calculated in DDD/1,000 insured/day and was statistically processed. RESULTS: The consumption of all statins increased by 194%, while the consumption of high-dose statins in patients over 65 increased by 296%. The number of all patients on statin therapy increased by 58%, the number of patients over 65 on statin therapy increased by 87%, and the number of patients over 65 on high-dose statins increased by 326%. 60% of all patients over 65 receiving high-dose statins were women. The most used high-dose statins were atorvastatin and simvastatin. CONCLUSION: Consumption of all statins increased, mostly high-dose statins in the 65+ age group, the most sensitive population for adverse effects. The number of 65+ patients on high-dose statins grew much faster than the general statin user group, thus increasing the risk potential. Women are dominating all age and dose groups of statin users.

[50] *DiBella M, Thomas MS, Alyousef H et al.* **Choline Intake as Supplement or as a Component of Eggs Increases Plasma Choline and Reduces Interleukin-6 without Modifying Plasma Cholesterol in Participants with Metabolic Syndrome**. Nutrients 2020; 12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33066009
ABSTRACT
Metabolic syndrome (MetS) is characterized by low-grade inflammation and insulin resistance, which increase the risk of heart disease. Eggs have numerous nutrients including choline, carotenoids, and fat-soluble vitamins that may protect against these conditions. Egg phosphatidylcholine (PC) is a major contributor of dietary choline in the American diet.

However, uncertainty remains regarding eggs due to their high concentration of cholesterol. In this study, we evaluated the effect of two sources of choline, whole eggs (a source of PC) and a choline supplement (choline bitartrate, CB), on plasma lipids, glucose, insulin resistance, and inflammatory biomarkers. We recruited 23 subjects with MetS to participate in this randomized cross-over intervention. After a 2-week washout, with no choline intake, participants were randomly allocated to consume three eggs/day or CB (~400 mg choline/d for both) for 4 weeks. After a 3-week washout period, they were allocated to the alternate treatment. Dietary records indicated higher concentrations of vitamin E and selenium during the egg period ($p < 0.01$). Interestingly, there were no changes in plasma total, low density lipoprotein (LDL)- or high density lipoprotein (HDL)-cholesterol, triglycerides, or glucose, compared either to baseline or between treatments. In contrast, interleukin-6 was reduced, with both sources of choline compared to baseline, while eggs also had an effect on lowering C-reactive protein, insulin, and insulin resistance compared to baseline. This study demonstrates that in a MetS population, intake of three eggs per day does not increase plasma LDL cholesterol, and has additional benefits on biomarkers of disease compared to a choline supplement, possibly due to the presence of other antioxidants in eggs.

[51] *Tan WYT, Young BE, Lye DC et al.* **Statin use is associated with lower disease severity in COVID-19 infection**. Scientific reports 2020; 10:17458.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33060704
ABSTRACT
We aim to study the association of hyperlipidemia and statin use with COVID-19 severity. We analysed a retrospective cohort of 717 patients admitted to a tertiary centre in Singapore for COVID-19 infection. Clinical outcomes of interest were oxygen saturation ≤ 94% requiring supplemental oxygen, intensive-care unit (ICU) admission, invasive mechanical-ventilation and death. Patients on long term dyslipidaemia medications (statins, fibrates or ezetimibe) were considered to have dyslipidaemia. Logistic regression models were used to study the association between dyslipidaemia and clinical outcomes adjusted for age, gender and ethnicity. Statin treatment effect was determined, in a nested case-control design, through logistic treatment models with 1:3 propensity matching for age, gender and ethnicity. All statistical tests were two-sided, and statistical significance was taken as $p < 0.05$. One hundred fifty-six (21.8%) patients had dyslipidaemia and 97% of these were on statins. Logistic treatment models showed a lower chance of ICU admission for statin users when compared to non-statin users (ATET: Coeff (risk difference): - 0.12 (- 0.23, - 0.01); $p = 0.028$). There were no other significant differences in other outcomes. Statin use was independently associated with lower ICU admission. This supports current practice to continue prescription of statins in COVID-19 patients.

[52] *Seitun S, Clemente A, Maffei E et al.* **Prognostic value of cardiac CT**. Radiol Med 2020; 125:1135-1147.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33047297
ABSTRACT
In the past decades, coronary computed tomography angiography (CCTA) has become a powerful tool in the management of coronary artery disease. The diagnostic and prognostic value of CCTA has been extensively demonstrated in both large observational studies and clinical trials among stable chest pain patients. The quantification of coronary artery calcium

score (CACS) is a well-established predictor of cardiovascular morbidity and mortality in asymptomatic subjects. Besides CACS, the main strength of CCTA is the accurate assessment of the individual total atherosclerotic plaque burden, which holds important prognostic information. In addition, CCTA, by providing detailed information on coronary plaque morphology and composition with identification of specific high-risk plaque features, may further improve the risk stratification beyond the assessment of coronary stenosis. The development of new CCTA applications, such as stress myocardial CT perfusion and computational fluids dynamic applied to standard CCTA to derive CT-based fractional flow reserve (FFR) values have shown promising results to guide revascularization, potentially improving clinical outcomes in stable chest pain patients. In this review, starting from the role of CACS and moving beyond coronary stenosis, we evaluate the existing evidence of the prognostic effectiveness of the CCTA strategy in real-world clinical practice.

[53] *Mahmood T, Shapiro MD*. **Coronary artery calcium testing in low-intermediate risk symptomatic patients with suspected coronary artery disease: An effective gatekeeper to further testing?** PloS one 2020; 15:e0240539.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33048982
ABSTRACT
Computed tomography for quantification of coronary artery calcium (CAC) is a simple non-invasive tool to assess atherosclerotic plaque burden. CAC is highly correlated with coronary atherosclerosis and is a robust predictor of cardiovascular outcomes. Recently, the 2018 ACC/AHA Cholesterol Guidelines endorsed the use of CAC scores in asymptomatic, intermediate risk individuals where the decision to initiate stain therapy is uncertain. However, whether quantification of CAC may play a role in the assessment of symptomatic individuals remains a matter of debate. In this review, we examine the evidence for the use of CAC in low-intermediate risk patients with chest pain. This appraisal places a particular focus on the growing body of literature supporting the negative predictive value of a CAC score of zero to rule out significant coronary artery disease in those without high-risk features. We also evaluate current guidelines, limitations, and future research directions for CAC scoring in this important subgroup of patients.

[54] *Hazer İ, Kabukçu HO, Yağcı M et al.* **The association of lipid metabolism and non-alcoholic fatty liver disease in children with obesity**. Turk Pediatri Ars 2020; 55:263-269.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33061754
ABSTRACT
AIM: Obesity, insulin resistance, and hyperlipidemia have been shown as risk factors for non-alcoholic fatty liver disease. In this study, the association between lipid and lipoprotein metabolism abnormalities and the presence of non-alcoholic fatty liver disease was investigated in patients with obesity. MATERIAL AND METHODS: In this study, the clinical, laboratory and imaging findings of 357 children and adolescent patients (199 girls and 158 boys) aged 2-18 years who were diagnosed as having obesity between 2013 and 2018 were retrospectively analyzed. The clinical and laboratory features of the patients who were diagnosed as having non-alcoholic fatty liver disease using ultrasonography were compared with patients who did not have non-alcoholic fatty liver disease. All lipid and lipoprotein levels were defined as hypo-, normo- and hyperlipidemic in comparison with the reference values according to age and sex. RESULTS: The frequency of non-alcoholic fatty liver disease was

44.5% in the entire study group and was higher in males (p<0.05). The body weight, body mass index, alanine aminotransferase, glucose, insulin, non-high-density lipoprotein-cholesterol, and HOMA-IR scores were found to be higher in the patients with non-alcoholic fatty liver disease, whereas the high-density lipoprotein-cholesterol level was lower (p<0.05). There was no difference in the frequency of non-alcoholic fatty liver disease among the patients with low, normal, and high total cholesterol, triglyceride and low-density lipoprotein-cholesterol levels (p>0.05). The frequency of lipid metabolism disorder (hypolipidemia and/or hyperlipidemia) was found as 77.5% in all patients. CONCLUSION: Non-alcoholic liver disease and lipid metabolism disorders are common in children and adolescents with obesity. The frequency of non-alcoholic fatty liver disease in hypolipidemic, normolipidemic, and hyperlipidemic patients was not different. This finding indicated that the increase in the amount of body fatty tissue and insulin resistance were more important risk factors in the development of non-alcoholic fatty liver disease.

[55] *Formanowicz D, Krawczyk JB*. **Controlling the thickness of the atherosclerotic plaque by statin medication**. PloS one 2020; 15:e0239953.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33048950
ABSTRACT
Atherosclerosis, a chronic inflammatory disorder of the arterial wall, is a complex process whose dynamics are affected by multiple factors. The disease control consists of restraining it by administering statins. Slowing down or halting the plaque growth depends on the patient age at which the statin treatment begins and on the thickness of the intima-media (IMT) at that time. In this paper, we propose a mathematical model to estimate the sets of atherosclerosis states, from which the use of statins can restrain the disease. Our model is control-theoretic, and the estimated sets are the viability kernels, in the parlance of viability theory. To our best knowledge, this way of modelling the atherosclerosis progression is original. We compute two viability kernels, each for a different statin-treatment dose. Each kernel is composed of the vector [age, IMT] from which the disease can be restrained. By extension, the disease can't be restrained from the kernel complements, this being mainly because of the disease and patient-age advancement. The kernels visualise tradeoffs between early and late treatments, which helps the clinician to decide when to start the statin treatment and which statin dose may be sufficient.

[56] *Dessie G, Tadesse Y, Demelash B, Genet S*. **Assessment of Serum Lipid Profiles and High-sensitivity C-reactive Protein Among Patients Suffering from Rheumatoid Arthritis at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: A Cross-Sectional Study**. Open Access Rheumatol 2020; 12:223-232.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33061690
ABSTRACT
BACKGROUND: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by severe joint pain, swelling, damage, and disability which leads to joint destruction and loss of function. The complication of RA is associated with cardiovascular diseases, particularly due to systemic inflammation and dyslipidemia. The purpose of this study was to assess the development of atherosclerosis, which acts as a major risk factor for cardiovascular complications in RA patients. METHODS: A hospital-based cross-sectional study was conducted at the Rheumatology Clinic of Tikur Anbessa Specialized Hospital. The study made

a comparison of risk factors (dyslipidemia and inflammatory status) between individuals having RA as a case group and apparently healthy individuals as a control group. Simple descriptive statistics, one-way ANOVA, independent sample t-test and multivariate analysis were utilized for statistical analysis. p-value of <0.05 at the 95% confidence level was considered as statistically significant. RESULTS: The result of this study demonstrated that there was a significant elevation of mean ±SD of TC, TC/HDL, LDL/HDL, and lowered value of HDL-C was seen among RA patients than controls (P-value <0.05). The mean ±SD of inflammatory marker, high-sensitivity C-reactive protein (hsCRP), was significantly higher among RA patients compared to controls (P<0.05). HDL-C had a significant negative correlation with a hsCRP whereas TC/HDL-C and LDL/HDL-C had a significant positive correlation with hsCRP (P<0.05). CONCLUSION: In this study, RA patients had lipid abnormalities and elevated systemic inflammation than controls. An increase in hsCRP and dyslipidemia status among RA patients indicates the possible development of an atherosclerotic event. Therefore, assessment of lipid profiles and hsCRP in early RA patients may be helpful to assess the possible development of cardiovascular complications.

[57] *Cyr Y, Bissonnette S, Lamantia V et al.* **White Adipose Tissue Surface Expression of LDLR and CD36 is Associated with Risk Factors for Type 2 Diabetes in Adults with Obesity**. Obesity (Silver Spring, Md.) 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33043593
ABSTRACT
OBJECTIVE: Human conditions with upregulated receptor uptake of low-density lipoproteins (LDL) are associated with diabetes risk, the reasons for which remain unexplored. LDL induce metabolic dysfunction in murine adipocytes. Thus, it was hypothesized that white adipose tissue (WAT) surface expression of LDL receptor (LDLR) and/or CD36 is associated with WAT and systemic metabolic dysfunction. Whether WAT LDLR and CD36 expression is predicted by plasma lipoprotein-related parameters was also explored. METHODS: This was a cross-sectional analysis of 31 nondiabetic adults (BMI > 25 kg/m(2)) assessed for WAT surface expression of LDLR and CD36 (immunohistochemistry), WAT function, WAT and systemic inflammation, postprandial fat metabolism, and insulin resistance (IR; hyperinsulinemic-euglycemic clamp). RESULTS: Fasting WAT surface expression of LDLR and CD36 was negatively associated with WAT function ((3) H-triglyceride storage, r = -0.45 and -0.66, respectively) and positively associated with plasma IL-1 receptor antagonist (r = 0.64 and 0.43, respectively). Their expression was suppressed 4 hours postprandially, and reduced LDLR was further associated with IR (M/I(clamp) , r = 0.61 women, r = 0.80 men). Plasma apolipoprotein B (apoB)-to-PCSK9 ratio predicted WAT surface expression of LDLR and CD36, WAT dysfunction, WAT NLRP3 inflammasome priming and disrupted cholesterol-sensing genes, and systemic IR independent of sex and body composition. CONCLUSIONS: Higher fasting and lower postprandial WAT surface expression of LDLR and CD36 is associated with WAT dysfunction, systemic inflammation, and IR in adults with overweight/obesity, anomalies that are predicted by higher plasma apoB-to-PCSK9 ratio.

[58] *Cicero AFG, D'Addato S, Borghi C*. **A Randomized, Double-Blinded, Placebo-Controlled, Clinical Study of the Effects of a Nutraceutical Combination (LEVELIP DUO(®)) on LDL Cholesterol Levels and Lipid Pattern in Subjects with Sub-Optimal Blood Cholesterol Levels (NATCOL Study)**. Nutrients 2020; 12.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33066334
ABSTRACT
Phytosterols and red yeast rice are largely studied cholesterol-lowering nutraceuticals, respectively inhibiting the bowel absorption and liver synthesis of cholesterol. Our aim was to test the effect of combined nutraceutical-containing phytosterols and red yeast rice vs. a placebo on the lipid profile. We performed a parallel arms, double-blind, placebo-controlled clinical trial, randomizing 88 moderately hypercholesterolemic subjects to treatment with a combined nutraceutical containing phytosterols (800 mg) and red yeast rice, standardized to contain 5 mg of monacolins from Monascus purpureus, with added niacin (27 mg) and policosanols (10 mg) (LEVELIP DUO(®)), or placebo. The mean LDL-Cholesterol (LDL-C) change at Week 8 was -32.5 ± 30.2 mg/dL (-19.8%) in the combined nutraceutical group and 2.5 ± 19.4 mg/dL (2.3%) in the placebo group. The estimated between-group difference of -39.2 mg/dL (95% CI: -48.6; -29.8) indicates a statistically significant difference between treatments in favor of the combined nutraceutical ($p < 0.0001$). Total Cholesterol (TC), non-HDL cholesterol (non-HDL-C), Apolipoprotein B, TC/HDL-C and LDL-C/HDL-C improved in a similar way in the combined nutraceutical group only. No significant changes in other clinical and laboratory parameters were observed. In conclusion, the tested combined nutraceutical was well tolerated, while significantly reducing the plasma levels of LDL-C, TC, non-HDL-C, ApoB, TC/HDL-C and LDL-C/HDL-C ratios in mildly hypercholesterolemic patients. Trial registration (ClinicalTrials.gov): NCT03739242.

[59] *Bang JI, Moon CM, Kim HO et al.* **Blood pool activity on F-18 FDG PET/CT as a possible imaging biomarker of metabolic syndrome**. Scientific reports 2020; 10:17367.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33060688
ABSTRACT
Association of blood pool (BP) and adipose tissue activity from F-18 fluorodeoxyglucose positron-emission tomography/computed tomography (FDG PET/CT) with the parameters of metabolic syndrome (MetS) and different MetS/obesity types were investigated. 245 subjects underwent FDG PET/CT scan for health check-ups were investigated retrospectively. Associations of BP (BP SUV: SUV(max), SUV(mean)), visceral (VAT SUV), and subcutaneous adipose tissue (SAT SUV) activity with parameters of MetS, body mass index (BMI), and lipid profiles were analyzed. MetS/obesity types were subdivided into metabolically healthy obese (MHO) and metabolically unhealthy obese (MUO). BP SUV was higher in subjects with MetS (t-test, $P < 0.005$), and was associated with MetS from multivariable binary logistic regression (OR 5.232 $P = 0.010$). BP SUV was statistically higher in MUO than in MHO ($P < 0.05$) along with blood pressure, triglycerides, and HDL-cholesterol. Multivariable binary logistic regression analysis showed MUO had higher blood pressure and BP SUV, while lower HDL-cholesterol relative to MHO after adjusting for triglycerides.

[60] **Expression of Concern: Simvastatin Reduces Endotoxin-Induced Acute Lung Injury by Decreasing Neutrophil Recruitment and Radical Formation**. PloS one 2020; 15:e0240344.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33057342
ABSTRACT

[61] *Xiao Z, Zhang Y, Kuang Y, Ma Q*. **Changes in plasma levels of RIPK1, RIPK3, and MLKL in patients with coronary atherosclerotic heart disease and its clinical predictive value**. Zhong nan da xue xue bao. Yi xue ban = Journal of Central South University. Medical sciences 2020; 45:1096-1103.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33051424

ABSTRACT
OBJECTIVES: Coronary atherosclerotic heart disease (CHD) is caused by coronary atherosclerosis, which leads to stenosis and even occlusion of the lumen, resulting in myocardial ischemia, and necrosis subsequently. Its prevalence has been high for a long time. The prevention and treatment of CHD are important. The study aimed to investigate the role of plasma levels of receptor-interacting protein kinase 1 (RIPK1), receptor-interacting protein kinase 3 (RIPK3), and mixed-lineage kinase domain-like protein (MLKL) in patients with CHD and its clinical predictive value. METHODS: A total of 190 patients with CHD who were diagnosed by coronary angiography and 70 healthy subjects in cardiovascular department from September 2015 to May 2017 were enrolled in this study. Patients with CHD were assigned into 4 groups: Patients with stable angina pectoris (SAP, n=46), patients with unstable angina pectoris (UAP, n=56), patients with non-ST-segment elevation myocardial infarction (NSTEMI, n=42), and patients with ST-segment elevation myocardial infarction (STEMI, n=46). Patients with CHD were assigned into a single-vessel lesion group, a double-vessel lesion group, and a multi-vessel lesion group according to the results of coronary angiography, and the severity of coronary artery stenosis was determined by Gensini score. Plasma levels of RIPK1, RIPK3, and MLKL were measured by enzyme-linked immunosorbent assay (ELISA). RESULTS: The plasma levels of RIPK1, RIPK3, and MLKL in patients with CHD were significantly higher than those in the controls ($P<0.05$). The plasma levels of RIPK1, RIPK3, and MLKL in the UAP group were significantly higher than those in the SAP group ($P<0.05$). The plasma levels of RIPK1, RIPK3, and MLKL in NSTEMI and STEMI group were significantly higher than those in the UAP group ($P<0.05$). There was no significant difference between the NSTEMI group and STEMI group ($P>0.05$). The plasma levels of RIPK1, RIPK3 and MLKL were significantly increased with numbers of coronary artery lesions ($P<0.05$), which were positively correlated with Gensini scores. The multivariate logistic regression analysis showed that plasma levels of RIPK1, RIPK3, and MLKL were independent risk factors for severe coronary artery stenosis.The average period of follow-up was 24 months after hospital discharge. The patients were divided into 2 groups according to whether they had major adverse cardiovascular events (MACE). Compared with patient without MACE, patient with MACE had higher levels of RIPK1, RIPK3, and MLKL ($P<0.05$). Receiver operator characteristic (ROC) curve analysis showed that the area under curve of RIPK1 was 0.72 ($P<0.001$), the area under curve of RIPK3 was 0.83 ($P<0.001$), and the area under curve of MLKL was 0.75 ($P<0.001$). CONCLUSIONS: Plasma levels of RIPK1, RIPK3, and MLKL are closely related to CHD, and they have predictive value for the prognosis evaluation for patients with CHD.

[62] *Thongtang N, Tangkittikasem N, Samaithongcharoen K et al.* **Effect of Switching from Low-Dose Simvastatin to High-Dose Atorvastatin on Glucose Homeostasis and Cognitive Function in Type 2 Diabetes**. Vascular health and risk management 2020; 16:367-377.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33061398

ABSTRACT
BACKGROUND: High-intensity statin is recommended in high-risk type 2 diabetes (T2D); however, statin dose dependently increases the risk of developing new-onset diabetes, can potentially worsen glycemic control in T2D, and may cause cognitive impairment. This study aimed to investigate the effect of statin intensification on glucose homeostasis and cognitive function in T2D. MATERIALS AND METHODS: T2D patients who were taking simvastatin ≤20 mg/day were randomized to continue taking the same dosage of simvastatin (low-dose simvastatin group; LS, n=63) for 12 weeks, or to change to atorvastatin 40 mg/day for 6 weeks, and if tolerated, atorvastatin was increased to 80 mg/day for 6 weeks (high-dose atorvastatin group; HS, n=62). Fasting plasma glucose (FPG), glycated hemoglobin (HbA(1c)), plasma insulin, homeostatic model assessment of insulin resistance (HOMA-IR) and of β-cell function (HOMA-B), cognitive functions using Montreal Cognitive Assessment (MoCA), and Trail Making Test (TMT) were assessed at baseline, 6 weeks, and 12 weeks. RESULTS: Mean age of patients was 58.8±8.9 years, and 72% were female. Mean baseline FPG and HbA(1c) were 124.0±27.5 mg/dl and 6.9±0.8%, respectively. No differences in baseline characteristics between groups were observed. Change in HbA(1c) from baseline in the LS and HS groups was -0.1% and +0.1% (p=0.03) at 6 weeks, and -0.1% and +0.1% (p=0.07) at 12 weeks. There were no significant differences in FPG, fasting plasma insulin, HOMA-B, HOMA-IR, MoCA score, or TMT between groups at 6 or 12 weeks. CONCLUSION: Switching from low-dose simvastatin to high-dose atorvastatin in T2D resulted in a slight increase in HbA(1c) (0.1%) without causing cognitive decline.

[63] *Lam A, Schwertner A, Katrivesis J et al.* **Atherectomy with balloon angioplasty compared to balloon angioplasty alone for the treatment of chronic limb threatening ischemia: A national surgical quality improvement program database analysis**. Vascular 2020; 28:747-755.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33045944

ABSTRACT
OBJECTIVES: To compare perioperative outcomes related to atherectomy with percutaneous transluminal angioplasty versus percutaneous transluminal angioplasty alone for the treatment of lower extremity chronic limb threatening ischemia using a national patient database. METHODS: Patients with chronic limb threatening ischemia treated with atherectomy and percutaneous transluminal angioplasty or percutaneous transluminal angioplasty alone from 2011 to 2016 in the National Surgical Quality Improvement Program database were identified. Primary outcomes were major adverse limb events (30-day untreated loss of patency, major reintervention, major amputation) and major adverse cardiac events (cardiac arrest, composite outcome of myocardial infarction or stroke). Secondary outcomes included 30-day mortality, length of stay, and any unplanned readmission within 30 days. Multivariate regression analyses were performed to determine independent predictors of outcome. Propensity score matched cohort analysis was performed. A p-value <0.05 was considered statistically significant. Subgroup analyses of femoropopliteal and infrapopliteal interventions were performed. RESULTS: In total, 2636 (77.2%) patients were treated with percutaneous transluminal angioplasty and 778 (22.8%) were treated with atherectomy and percutaneous transluminal angioplasty. Multivariate analyses of the unadjusted cohort revealed no significant differences in major adverse cardiac events or major adverse limb events between the two groups (p-value >0.05). Subgroup analysis of femoropopliteal interventions demonstrated a

significantly decreased likelihood of untreated loss of patency in 30 days in the atherectomy group compared to the percutaneous transluminal angioplasty group (1.1% vs. 2.7%, respectively; p-value = 0.034), which persisted on propensity score matched analysis (1.1% vs. 3.1%, respectively; p-value = 0.026). CONCLUSION: Atherectomy with balloon angioplasty of femoropopliteal disease provides a significant decrease in untreated loss of patency compared to balloon angioplasty alone.