Literature update week 13 (2020)

[1] *Hermans MP, Ahn SA, Rousseau MF*. **Lipid and cardiometabolic features of T2DM patients achieving stricter LDL-C and non-HDL-C targets in accordance with ESC/EAS 2019 guidelines**. Acta Cardiol 2020:1-9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32202204
ABSTRACT
Background: New recommendations call for lowering LDL-C < 55 mg/dL and non-HDL-C < 85 mg/dL in very-high cardiovascular risk (VH-CVR) patients with type 2 diabetes (T2DM). This study assessed the proportion of VH-CVR diabetics currently meeting these primary and secondary lipid targets, and which therapies/phenotypes predict combined goals achievement.Methods: We analysed the cardiometabolic phenotype, use of lipid-modulatind drugs (LMD), pre- and post-LMD lipids levels, and CV complications among 1196 T2DM with high (n = 221; 18%) or VH-CVR (n = 975; 82%). Among the latter, the characteristics of combined lipid goal-achievers (n = 158) were compared to those of non-achievers (n = 817), with subgroup analyses of on-statin patients (n = 732) and those with established CVD taking statins (n = 362). Presence of statin-associated muscle symptoms (SAMS) was also recorded.Results: 75% of VH-CVR patients were on statins. Both LDL-C and non-HDL-C goals were achieved by 16.2% of all VH-CVR, 19.3% of on-statin VH-CVR, and 24.3% of patients with established CVD taking statins. Achieving both targets was associated with high-intensity statins, specifically rosuvastatin, [statin + ezetimibe] combination, lower baseline LDL-C, smaller LDLs, lower TG and lipoprotein(a), and reduced metabolic syndrome frequency. SAMS reporting did not differ between achievers and non-achievers.Conclusions: More than 80% of patients are above targets. To bridge this gap, apart from treating more LMD-naive/refractory diabetics, one should consider for LDL-C to put most patients on high-intensity statins, more often with ezetimibe and, within statins, to switch preferably to rosuvastatin. As regards non-HDL-C, the off-target patients' phenotype suggests that intensifying lifestyle measures against metabolic syndrome should supplement current therapies.

[2] *Sabouret P, Angoulvant D, Ray KK*. **Lipoprotein(a), the rediscovered risk factor, or how to get "back to the future"**. Archives of cardiovascular diseases 2020; 113:147-151.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32205042
ABSTRACT

[3] *Moradi N, Fadaei R, Rashidbeygi E et al.* **Evaluation of changing the pattern of CTRP5 and inflammatory markers levels in patients with coronary artery disease and type 2 diabetes mellitus**. Archives of physiology and biochemistry 2020:1-6.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32202952
ABSTRACT
Purpose: It has recently found that adipokines, play a numerous functional roles in inflammation, lipids and glucose metabolism and in the pathogenically conditions such as atherosclerosis and insulin resistance. Therefore, for the first time we aimed the present study to evaluating serum levels of CTRP5 and inflammatory cytokines patients with CAD and T2DM in comparison with controls.Methods: This study was done on 44 patients with CAD, 45 type 2 diabetes mellitus (T2DM), 41 CAD + T2DM and 41 controls. Serum levels of TNF-alpha, IL-6, MCP-1 and CTRP5 were investigated by ELISA method.Results: The CTRP5 levels of all patients groups were lower in comparison with control group. There was a significant negative relationship between CTRP5 levels

and cytokines concentration in the studied patients.Conclusions: Our findings suggested a potential role of CTRP5 in inflammatory process of underlying atherosclerosis and diabetes; however, more studies are needed to support these finding.

[4] *Dong W, Su X, Xu M et al.* **Preparation, characterization, and in vitro/vivo evaluation of polymer-assisting formulation of atorvastatin calcium based on solid dispersion technique**. Asian J Pharm Sci 2018; 13:546-554.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32211078
ABSTRACT
Due to low solubility and bioavailability, atorvastatin calcium is confronted with challenge in conceiving appropriate formulation. Solid dispersion of atorvastatin calcium was prepared through the solvent evaporation method, with Poloxamer 188 as hydrophilic carriers. This formulation was then characterized by scanning electron microscopy, differential scanning calorimetry, powder X-ray diffraction and fourier transform infrared spectroscopy. Moreover, all these studies suggested the conversion of crystalline atorvastatin calcium. In addition, the drug solubility studies as well as dissolution rates compared with bulk drug and market tablets Lipitor were also examined. Furthermore, the study investigated the pharmacokinetics after oral administration of Lipitor and solid dispersion. And the AUC0-8 h and Cmax increased after taking ATC-P188 solid dispersion orally compared with that of Lipitor. All these could be demonstrated that ATC-P188 solid dispersions would be prospective means for enhancing higher oral bioavailability of ATC.

[5] *Konishi K, Miyake T, Furukawa S et al.* **Advanced fibrosis of non-alcoholic steatohepatitis affects the significance of lipoprotein(a) as a cardiovascular risk factor**. Atherosclerosis 2020; 299:32-37.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32203743
ABSTRACT
BACKGROUND AND AIMS: Lipoprotein(a) [Lp(a)] is an important independent cardiovascular risk factor. However, Lp(a) levels are lower in patients with chronic liver disease than in healthy subjects. Furthermore, Lp(a) levels decrease as residual liver function declines. Although non-alcoholic fatty liver disease (NAFLD), especially advanced non-alcoholic steatohepatitis (NASH), increases the risk of cardiovascular diseases, the relationship between serum Lp(a) level and NASH is unknown. Thus, we examined the relationship between serum Lp(a) levels and biopsy-proved NAFLD and clarified the significance of Lp(a) measurements for cardiovascular disease screening in patients with NAFLD. METHODS: A total of 176 patients with NAFLD were enrolled. Comprehensive blood chemistry tests and histological examinations of liver samples were conducted. The relationship between serum Lp(a) levels and NAFLD was analyzed. RESULTS: Serum Lp(a) levels in advanced fibrosis (stage 3-4) were lower than those in non-advanced fibrosis (stage 0-2) ($p < 0.05$). After adjustment for age, sex, body mass index, alanine aminotransferase (ALT), creatinine (Cre), HbA1c level, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), and the use of lipid-lowering agents, the significant inverse association between advanced fibrosis and serum Lp(a) levels remained ($p < 0.01$). Although the Lp(a) level was inversely associated with an NAFLD Activity Score (NAS) of 5-8, there was no significant association between Lp(a) levels and NAS adjusted for age, sex, body mass index, ALT, Cre, HbA1c level, HDL-C,

LDL-C, TG, and the use of lipid-lowering agents. CONCLUSIONS: Advanced NASH is associated with low serum Lp(a) levels; therefore, Lp(a) levels may not be useful in evaluating cardiovascular risk.

[6] *Wu T, Sun J, Tan L et al.* **Enhanced osteogenesis and therapy of osteoporosis using simvastatin loaded hybrid system**. Bioact Mater 2020; 5:348-357.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32206736
ABSTRACT
Postmenopausal osteoporosis is a common chronic dynamic bone disorder, caused by estrogen deficiency. To address this issue, we constructed a controlled drug-release system composed of poly (N-isopropylacrylamide) brush modified mesoporous hydroxyapatite (MHA-SIM-P) loaded with simvastatin (SIM) using an ovariectomised (OVX) rat model. Quantitative alkaline phosphatase activity assay, alizarin red staining and RT-PCR were tested to evaluate the osteogenic ability in vitro. The results showed that the MHA-SIM-P nanoparticles significantly improved the osteogenic differentiation of OVX bone marrow stromal cells (BMSCs) in vitro. In osteoporotic animal model, the therapeutic efficiency for bone defect was evaluated by muCT analysis, tartrate-resistant acid phosphatase, haematoxylin and eosin staining, which showed improved bone formation and less osteoclastic response in OVX rats after surgery for 3 and 6 weeks. This polymer brush modified MHA system provided a sustained release system of hydrophobic SIM to inhibit osteoporosis together with MHA nanoparticle promoting the osteogenesis. Thus, this novel strategy exhibited great potential for promoting osteogenic ability and treating local osteoporotic defects.

[7] *Barra NG, Henriksbo BD, Anhe FF, Schertzer JD*. **The NLRP3 inflammasome regulates adipose tissue metabolism**. The Biochemical journal 2020; 477:1089-1107.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32202638
ABSTRACT
Adipose tissue regulates metabolic homeostasis by participating in endocrine and immune responses in addition to storing and releasing lipids from adipocytes. Obesity skews adipose tissue adipokine responses and degrades the coordination of adipocyte lipogenesis and lipolysis. These defects in adipose tissue metabolism can promote ectopic lipid deposition and inflammation in insulin-sensitive tissues such as skeletal muscle and liver. Sustained caloric excess can expand white adipose tissue to a point of maladaptation exacerbating both local and systemic inflammation. Multiple sources, instigators and propagators of adipose tissue inflammation occur during obesity. Cross-talk between professional immune cells (i.e. macrophages) and metabolic cells (i.e. adipocytes) promote adipose tissue inflammation during metabolic stress (i.e. metaflammation). Metabolic stress and endogenous danger signals can engage pathogen recognition receptors (PRRs) of the innate immune system thereby activating pro-inflammatory and stress pathways in adipose tissue. The Nod-like receptor protein 3 (NLRP3) inflammasome can act as a metabolic danger sensor to a wide range of pathogen- and damage-associated molecular patterns (PAMPs and DAMPs). Activation of the NLRP3 inflammasome facilitates caspase-1 dependent production of the pro-inflammatory cytokines IL-1beta and IL-18. Activation of the NLRP3 inflammasome can promote inflammation and pyroptotic cell death, but caspase-1 is also involved in adipogenesis. This review discusses the role of the NLRP3 inflammasome in adipose tissue immunometabolism responses relevant to metabolic disease. Understanding the potential sources of NLRP3 activation

and consequences of NLRP3 effectors may reveal therapeutic opportunities to break or fine-tune the connection between metabolism and inflammation in adipose tissue during obesity.

[8] *Bamji AN*. **Do PCSK9 inhibitors do anything more than reduce LDL cholesterol?** Bmj 2020; 368:m1159.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32209543
ABSTRACT

[9] *Brownstein AJ, Martin SS*. **More accurate LDL-C calculation: Externally validated, guideline endorsed**. Clinica chimica acta; international journal of clinical chemistry 2020; 506:149-153.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32205096
ABSTRACT
Low density lipoprotein-cholesterol (LDL-C) serves as the primary target of therapy for preventing atherosclerotic cardiovascular disease (ASCVD). Recently released European and American guidelines on lipid management recommend attaining very low LDL-C levels (<1.8 mmol/L or even lower) in high and very-high risk patients. Therefore, utilizing an accurate means for determining LDL-C, especially at such low values, is of paramount importance to inform the best clinical decisions and use of effective therapies. This review compares the different methods of determining LDL-C, including the various forms of direct measurement and most commonly used calculations. This review discusses the evidence behind these methods in different populations of patients and in the fasting versus non-fasting state. The Martin/Hopkins method is the preferred method for determining LDL-C as it is the most accurate and widely applicable method. It is especially useful in patients with low LDL-C levels < 1.8 mmol/L (<70 mg/dL) and high triglyceride levels between 1.7 and 4.5 mmol/L (150-399 mg/dL), and is reliable in the non-fasting state.

[10] *Chen YQ, Zhao SP, Ye HJ*. **Efficacy and safety of coenzyme A versus fenofibrate in patients with hyperlipidemia: a multicenter, double-blind, double-mimic, randomized clinical trial**. Current medical research and opinion 2020:1-5.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32212983
ABSTRACT
Background: We investigated the lipid-lowering efficacy and safety of coenzyme A (CoA) versus fenofibrate in Chinese patients with moderate dyslipidemia.Methods: A total of 417 subjects (aged 18-75 years) diagnosed with moderate dyslipidemia (triglyceride 2.3-6.5 mmol/L) from 13 large cardiovascular centers in China were recruited and randomly divided into a fenofibrate group (n = 207), which received 200 mg of fenofibrate orally once daily, and a CoA group (n = 210), which received 400 mg of CoA orally once a day. Blood lipoproteins, liver and renal function, creatine kinase, and blood glucose were measured at baseline, and after 4 and 8 weeks of treatment.Results: The baseline triglyceride (TG) level in the fenofibrate group and the CoA group was 3.39 +/- 0.99 mmol/L and 3.60 +/- 1.11 mmol/L, respectively. After treatment for 4 and 8 weeks with fenofibrate, TG was reduced by 31.62% and 33.13%. In the CoA group, TG was reduced by 17.29% and 23.80%. Compared with baseline, total cholesterol (TC) was significantly decreased in both groups after either 4 or 8 weeks of treatment ($p < .05$). CoA increased high-density lipoprotein cholesterol (HDL-C) after 4 weeks of treatment, whereas it had no significant effect on HDL-C after 8 weeks of treatment. Low-density lipoprotein cholesterol (LDL-C) was not modified in

either group. The incidence of side effects was significantly lower in the CoA group compared with the fenofibrate group ($p < .05$).Conclusions: Compared with fenofibrate, CoA has less effect on reducing plasma TG levels in subjects with moderate dyslipidemia. However, it has fewer adverse effects.

[11] *Katdare A, Khunt D, Thakkar S et al.* **Comparative evaluation of fish oil and butter oil in modulating delivery of galantamine hydrobromide to brain via intranasal route: pharmacokinetic and oxidative stress studies**. Drug delivery and translational research 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32219727
ABSTRACT
The present study investigates the role of fish oil (FO)- and butter oil (BO)-enriched microemulsion-based system of galantamine hydrobromide (GH), an anti-Alzheimer drug, for its potential role in brain permeation enhancement and neuroprotection against oxidative stress. Microemulsion (ME)-based system of GH was prepared using water phase titration. The prepared ME was characterized by several physicochemical parameters like particle size, polydispersity index, and ex vivo drug permeation. Cell-based oxidative stress assays and pharmacokinetic studies were performed using C6 glial cell lines, and Sprague Dawley rats, respectively. The optimized ME comprised 5.3% v/v of Capmul MCM EP (as oil),15.8% v/v of Tween-80 (as surfactant), 5.3% v/v of Transcutol P (as co-surfactant), and 73.6% v/v of water (as aqueous phase). The addition of FO and BO resulted in a slight increase in the droplet size and decrease in transparency of ME. Cell-based anti-oxidative stress assays (glutathione assay, nitrite assay, and lipid peroxidation assay) showed the efficacy of formulation in the order of ME, BO ME, and FO ME, respectively. A similar trend was also observed in in vivo animal studies, wherein GH FO ME showed a comparatively higher percentage of drug reaching the brain when administered by intranasal route than by IV route. The study concluded the potential benefits of co-administering FO- and BO-enriched microemulsion is not only enhancing the permeation of drugs across BBB but also improving efficacy against lipopolysaccharide-induced oxidative stress. Graphical abstract.

[12] *Riu DS, Sunarno I, Lukas E et al.* **The effect of pravastatin on endothelin-1 levels and pregnancy outcomes in women who have a high risk for preeclampsia: A randomized control trial**. Enferm Clin 2020; 30 Suppl 2:499-505.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32204222
ABSTRACT
OBJECTIVE: This study aimed to evaluate the effect of aspirin and pravastatin compared with aspirin on endothelin-1 levels, and the pregnancy outcome in pregnant women high risk for preeclampsia. METHODS: It was a randomized clinical trial (RCT) analysis with block permutation. The sample divided into two groups. Group A as control has given aspirin 80mg and group B as an intervention group given aspirin 80mg plus pravastatin 20mg twice daily until 35 weeks gestation. Level of Endothelin-1 examined before and after treatment. RESULTS: There no differences found in endothelin-1 levels before and after being treated with aspirin or aspirin and pravastatin, as well as in the umbilical artery resistance index, fetal biometry, and the development of the fetus in two groups was typical at 28-32 weeks' gestation. Similarly, no differences found in fetal outcomes such as preterm birth, fetal growth retardation, and the incidence of preeclampsia between the two groups. CONCLUSION: As a conclusion, the administration of pravastatin, together with aspirin is no

more effective than aspirin in preventing preeclampsia, to pregnancy outcome and decreasing endothelin-1 levels. No congenital abnormalities reported.

[13] *Rausch C, Hoffmann F*. **Prescribing medications of questionable benefit prior to death: a retrospective study on older nursing home residents with and without dementia in Germany**. Eur J Clin Pharmacol 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32219538
ABSTRACT
PURPOSE: We studied the prevalence of medications of questionable benefit in the last 6 months of life among older nursing home residents with and without dementia in Germany. METHODS: A retrospective cohort study was conducted on claims data from 67,328 deceased nursing home residents aged 65+ years who were admitted between 2010 and 2014. We analyzed prescription regimens of medications of questionable benefit in the 180-91-day period and the 90-day period prior to death for residents with dementia (n = 29,052) and without dementia (n = 38,276). Factors associated with new prescriptions of medications of questionable benefit prior to death were analyzed using logistic regression models among all nursing home residents and stratified by dementia. RESULTS: A higher proportion of nursing home residents with dementia were prescribed at least one medication of questionable benefit in the 180-91-day (29.6%) and 90-day (26.8%) periods prior to death, compared with residents without dementia (180-91 days, 22.8%; 90 days, 20.1%). Lipid-lowering agents were the most commonly prescribed medications. New prescriptions of medications of questionable benefit were more common among residents with dementia (9.8% vs. 8.7%). When excluding anti-dementia medication, new prescriptions of these medications were more common among residents without dementia (6.4% vs. 8.0%). The presence of dementia (odds ratio [OR] 1.40, 95% confidence interval [95%CI] 1.32-1.48) and excessive polypharmacy were associated with new prescriptions of medications of questionable benefit prior to death (OR 4.74, 95%CI 4.15-5.42). CONCLUSION: Even when accounting for anti-dementia prescriptions, the prevalence of nursing home residents with dementia receiving medications of questionable benefit is considerable and may require further attention.

[14] *Nicholls SJ, Bubb K*. **The mystery of evacetrapib - why are CETP inhibitors failing?** Expert review of cardiovascular therapy 2020; 18:127-130.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32200670
ABSTRACT

[15] *Baptista LC, Sun Y, Carter CS, Buford TW*. **Crosstalk Between the Gut Microbiome and Bioactive Lipids: Therapeutic Targets in Cognitive Frailty**. Front Nutr 2020; 7:17.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32219095
ABSTRACT
Cognitive frailty is a geriatric condition defined by the coexistence of cognitive impairment and physical frailty. This "composite" aging phenotype is associated with a higher risk of several adverse health-related outcomes, including dementia. In the last decade, cognitive frailty has gained increased attention from the scientific community that has focused on understanding the clinical impact and the physiological and pathological mechanisms of development and on identifying preventive and/or rehabilitative therapeutic interventions. The emergence of gut microbiome in

neural signaling increased the interest in targeting the gut-brain axis as a modulation strategy. Multiple studies on gastroenteric, metabolic, and neurodegenerative diseases support the existence of a wide bidirectional communication network of signaling mediators, e.g., bioactive lipids, that can modulate inflammation, gut permeability, microbiota composition, and the gut-brain axis. This crosstalk between the gut-brain axis, microbiome, and bioactive lipids may emerge as the basis of a promising therapeutic strategy to counteract cognitive frailty. In this review, we summarize the evidence in the literature regarding the link between the gut microbiome, brain, and several families of bioactive lipids. In addition, we also explore the applicability of several bioactive lipid members as a potential routes for therapeutic interventions to combat cognitive frailty.

[16] *Arbeev KG, Bagley O, Ukraintseva SV et al.* **Composite Measure of Physiological Dysregulation as a Predictor of Mortality: The Long Life Family Study**. Frontiers in public health 2020; 8:56.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32211364
ABSTRACT
Biological aging results in changes in an organism that accumulate over age in a complex fashion across different regulatory systems, and their cumulative effect manifests in increased physiological dysregulation (PD) and declining robustness and resilience that increase risks of health disorders and death. Several composite measures involving multiple biomarkers that capture complex effects of aging have been proposed. We applied one such approach, the Mahalanobis distance (DM), to baseline measurements of various biomarkers (inflammation, hematological, diabetes-associated, lipids, endocrine, renal) in 3,279 participants from the Long Life Family Study (LLFS) with complete biomarker data. We used DM to estimate the level of PD by summarizing information about multiple deviations of biomarkers from specified "norms" in the reference population (here, LLFS participants younger than 60 years at baseline). An increase in DM was associated with significantly higher mortality risk (hazard ratio per standard deviation of DM: 1.42; 95% confidence interval: [1.3, 1.54]), even after adjustment for a composite measure summarizing 85 health-related deficits (disabilities, diseases, less severe symptoms), age, and other covariates. Such composite measures significantly improved mortality predictions especially in the subsample of participants from families enriched for exceptional longevity (the areas under the receiver operating characteristic curves are 0.88 vs. 0.85, in models with and without the composite measures, p = 2.9 x 10(-5)). Sensitivity analyses confirmed that our conclusions are not sensitive to different aspects of computational procedures. Our findings provide the first evidence of association of PD with mortality and its predictive performance in a unique sample selected for exceptional familial longevity.

[17] *Lettino M, Zambon A, Musumeci G et al.* **[Appropriateness criteria for the management of lipid-lowering therapy with alirocumab in high cardiovascular risk patients. The opinion of a multidisciplinary group of Italian experts]**. Giornale italiano di cardiologia (2006) 2020; 21:3s-21s.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32202541
ABSTRACT
High levels of LDL cholesterol (LDL-C) represent a causal factor for cardiovascular diseases on an atherosclerotic basis, with a direct correlation between these and mortality or cardiovascular events, such that the reduction of both is associated proportionally and linearly with the reduction

of LDL-C.Statins and ezetimibe are used for LDL-C lowering but may not be sufficient to achieve the targets defined by the ESC/EAS guidelines, which recommend use of PCSK9 inhibitors for further LDL-C reduction in patients not at goal.This project submitted 86 clinical scenarios to a group of experts, cardiologists, internists and lipidologists, collecting their opinion on the appropriateness of different behaviors and decisions. We used the RAND/UCLA method of assessing the appropriateness of clinical interventions, validated to combine the best scientific evidence available with expert judgment. To this end, the benefit-risk ratio was evaluated in the proposed clinical scenarios. Each indication was classified as "appropriate", "uncertain" or "inappropriate" based on the average score given by the participants.This document presents the results of a consensus process that led to the development of recommendations for the management of clinical scenarios on the treatment of patients with dyslipidemia, which cannot always be solved with scientific evidence alone.

[18] *Lucchi T, Cesari M, Vergani C*. **[Lipid-lowering therapy for the prevention of atherosclerotic cardiovascular disease: guidelines and clinical practice]**. Giornale italiano di cardiologia (2006) 2020; 21:256-263.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32202556
ABSTRACT

[19] *Masiero G, Franzone A, Silvestri T et al.* **[PCSK9 inhibitor use in high cardiovascular risk patients: an interventionalist's overview on efficacy, current recommendations and factual prescription]**. Giornale italiano di cardiologia (2006) 2020; 21:264-270.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32202557
ABSTRACT

[20] *Wicinski M, Gorski K, Wodkiewicz E et al.* **Vasculoprotective Effects of Vildagliptin. Focus on Atherogenesis**. International journal of molecular sciences 2020; 21.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32218354
ABSTRACT
Vildagliptin is a representative of Dipeptidyl Peptidase-4 (DPP-4) inhibitors, antihyperglycemic drugs, approved for use as monotherapy and combination therapy in type 2 diabetes mellitus. By inhibiting enzymatic decomposition, DPP-4 inhibitors increase the half-life of incretins such as GLP-1 (Glucagon-like peptide-1) and GIP (Gastric inhibitors polypeptide) and prolong their action. Some studies present results suggesting the anti-sclerotic and vasculoprotective effects of vildagliptin reaching beyond glycemic control. Vildagliptin is able to limit inflammation by suppression of the NF-kappaB (nuclear factor kappa-light-chain-enhancer of activated B cells) signaling pathway and proinflammatory agents such as TNF-alpha (tumor necrosis factor alpha), IL-1beta (Interleukin-1beta), and IL-8 (Interleukin 8). Moreover, vildagliptin regulates lipid metabolism; attenuates postprandial hypertriglyceridemia; and lowers serum triglycerides, apolipoprotein B, and blood total cholesterol levels. This DPP-4 inhibitor also reduces macrophage foam cell formation, which plays a key role in atheromatous plaque formation and stability. Vildagliptin reduces vascular stiffness via elevation of nitric oxide synthesis, improves vascular relaxation, and results in reduction in both systolic and diastolic blood pressure. Treatment with vildagliptin lowers the level of PAI-1 presenting possible antithrombotic effect. By affecting the endothelium, inflammation,

and lipid metabolism, vildagliptin may affect the development of atherosclerosis at its various stages. The article presents a summary of the studies assessing vasculoprotective effects of vildagliptin with special emphasis on atherogenesis.

[21] *Zhao B, Li X, Xu H et al.* **Influence of Simvastatin-Strontium-Hydroxyapatite Coated Implant Formed by Micro-Arc Oxidation and Immersion Method on Osteointegration in Osteoporotic Rabbits**. International journal of nanomedicine 2020; 15:1797-1807.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32214812
ABSTRACT
Purpose: Enhancing osteointegration of implants in osteoporosis patients is a necessity since implantations frequently fail in these patients. The aim of this work is to study how simvastatin-strontium-hydroxyapatite coated implants perform in rabbits with osteoporosis. Materials and Methods: Crystalline HA and Sr-HA oxide film were prepared through micro-arc oxidation. Surface characterization including morphology, roughness, element composition, phase composition, hydrophilicity were then evaluated. Simvastatin loaded on porous films through immersion, and the effects of coatings on osteointegration in osteoporotic rabbits were investigated. All samples were obtained after 4, 8 and 12 weeks of healing. Some of them were subjected to biomechanical tests and others were subjected to histological and histomorphometric analysis. Results: Coatings exhibited a microporous network structure with appropriate roughness and high hydrophilicity. Compared to control HA and machined surface implants, simvastatin-Sr-HA coated implants exhibited marked improvements in osteointegration, which is characterized by a quicker mineralization deposition rate, good bone formation mode (large amount of contact osteogenesis and a small amount of distance osteogenesis) and increased bone-to-implant contact and pull-out strength. Conclusion: These biological parameters demonstrate the excellent osteoconductivity of simvastatin-Sr-HA coatings in the osteoporotic state. Overall, this suggests that simvastatin-Sr-HA coatings would be applicable in poor-quality bones of patients experiencing osteoporosis.

[22] *Burnap SA, Joshi A, Tsimikas S et al.* **High-Density Lipoproteins Are the Main Carriers of PCSK9 in the Circulation**. Journal of the American College of Cardiology 2020; 75:1495-1497.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32216920
ABSTRACT

[23] *Mendieta G, Ben-Aicha S, Gutierrez M et al.* **Intravenous Statin Administration During Myocardial Infarction Compared With Oral Post-Infarct Administration**. Journal of the American College of Cardiology 2020; 75:1386-1402.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32216907
ABSTRACT
BACKGROUND: Beyond lipid-lowering, statins exert cardioprotective effects. High-dose statin treatment seems to reduce cardiovascular complications in high-risk patients. The ideal timing and administration regime remain unknown. OBJECTIVES: This study compared the cardioprotective effects of intravenous statin administration during myocardial infarction (MI) with oral administration immediately post-MI. METHODS: Hypercholesterolemic pigs underwent MI induction (90 min of ischemia) and were kept for 42 days. Animals were distributed in 3 arms (A): A1 received an intravenous bolus of atorvastatin during MI; A2 received an intravenous bolus of

vehicle during MI; and A3 received oral atorvastatin within 2 h post-MI. A1 and A3 remained on daily oral atorvastatin for the following 42 days. Cardiac magnetic resonance analysis (days 3 and 42 post-MI) and molecular/histological studies were performed. RESULTS: At day 3, A1 showed a 10% reduction in infarct size compared with A3 and A2 and a 50% increase in myocardial salvage. At day 42, both A1 and A3 showed a significant decrease in scar size versus A2; however, A1 showed a further 24% reduction versus A3. Functional analyses revealed improved systolic performance in A1 compared with A2 and less wall motion abnormalities in the jeopardized myocardium versus both groups at day 42. A1 showed enhanced collagen content and AMP-activated protein kinase activation in the scar, increased vessel density in the penumbra, higher tumor necrosis factor alpha plasma levels and lower peripheral blood mononuclear cell activation versus both groups. CONCLUSIONS: Intravenous administration of atorvastatin during MI limits cardiac damage, improves cardiac function, and mitigates remodeling to a larger extent than when administered orally shortly after reperfusion. This therapeutic approach deserves to be investigated in ST-segment elevation MI patients.

[24] *Ferreira JP, Xhaard C, Lamiral Z et al.* **PCSK9 Protein and rs562556 Polymorphism Are Associated With Arterial Plaques in Healthy Middle-Aged Population: The STANISLAS Cohort**. Journal of the American Heart Association 2020; 9:e014758.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32208829

ABSTRACT

Background PCSK9 (Proprotein convertase subtilisin/kexin type 9) binds low-density lipoprotein receptor, preventing its recycling. PCSK9 is a risk predictor and a biotarget in atherosclerosis. The PCSK9-rs562556 variant has been reported as a gain-of-function mutation. The aim of this study was to determine whether the PCSK9-low-density lipoprotein receptor-rs562556 axis is associated with carotid artery plaques between 2 visits separated by almost 20 years in a longitudinal population cohort. Methods and Results The STANISLAS (Suivi Temporaire Annuel Non-Invasif de la Sante des Lorrains Assures Sociaux) cohort is a longitudinal familial cohort from the Lorraine region of France. Participants attending 2 visits (visit 1 and visit 4) separated by 18.5 years (mean) were included (n=997). Carotid artery plaques were determined with standardized vascular echography. The mean age of the adult population at visit 1 was 42+/-5 years. At visit 4, 203 (20.4%) participants had arterial plaques. Participants who developed arterial plaques were older (42.7+/-5.4 versus 41.7+/-4.7 years), more often male (60% versus 49%), smokers (29% versus 18%), with diabetes mellitus (6% versus 3%), and higher cholesterol levels (low-density lipoprotein cholesterol, 1.6+/-0.4 versus 1.5+/-0.3 g/L) (all P<0.05). The independent factors associated with arterial plaques were age, smoking, and low-density lipoprotein cholesterol. Higher PCSK9 levels were associated with arterial plaques on top of the clinical model (odds ratio, 2.14; 95% CI,= 1.28-3.58); the missense mutation coding the single-nucleotide polymorphism rs562556 was associated with both higher PCSK9 concentration and incident carotid arterial plaques. Conclusions Higher PCSK9 concentration was associated with the development of arterial plaques almost 20 years in advance in a healthy middle-aged population. Mutations of the single-nucleotide polymorphism rs562556 associated with both PCSK9 levels and arterial plaques reinforce the potential causality of our findings. PCSK9 inhibitors could be useful for primary cardiovascular prevention.

[25] *Lauridsen C.* **Effects of dietary fatty acids on gut health and function of pigs pre- and post-weaning**. Journal of animal science 2020; 98.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32215565
ABSTRACT
Fatty acids (FA) play a major role in relation to mucosal immune responses, epithelial barrier functions, oxidative stress, and inflammatory reactions. The dietary FA composition and the molecular structures (chain length and number of double bonds) influence digestion, absorption and metabolism, and the bioactivity of the FA. Piglets post-weaning having an immature intestine and not fully formed immune functions are very vulnerable to invading microorganisms. Manipulation of the milk FA composition via sow nutrition, or inclusion of dietary fat sources in the feed for newly weaned pigs, may be used as a strategic tool to enhance pig performance and their gut health and function pre- and post-weaning. Medium-chain fatty acids (MCFA) are absorbed directly into the portal blood and may contribute to immediate energy for the enterocytes. In addition, the MCFA, similarly to the short-chain fatty acids (SCFA), possess antibacterial effects and may thereby prevent overgrowth of pathogenic bacteria in the gastrointestinal tract. The essential FA, linoleic (LA) and alpha-linolenic (ALA) FA, form the building blocks for the long-chain polyunsaturated n-3 and n-6 FA. The conversion of ALA and LA into n-3 and n-6 eicosanoids, respectively, influences the molecular structures of metabolites and inflammatory reactions and other immune responses upon bacterial challenges. Dietary manipulation of the lactating sow influences the transfer of the n-3 and n-6 polyunsaturated fatty acids (PUFA) from the sow milk to the piglet and the incorporation of the FA into piglet enteric tissues and cell membranes, which exerts bioactivity of importance for immune responses and the epithelial barrier function. Especially, the n-3 PUFA present in fish oil seem to influence the gut health and function of pigs, and this is of importance during the transition periods such as post-weaning in which piglets are prone to inflammation. The proportion of unsaturated FA in the cell membranes influences the susceptibility to oxidative stress. Oxidative stress accompanies infectious diseases, and the development of lipid peroxides and other reactive oxygen products may be harmful to the epithelial barrier function. Fatty acid peroxides from the feed may also be absorbed with other lipid-solubles and thereby harm the intestinal function. Hence, antioxidative protection is important for the enteric cells. In conclusion, manipulation of the dietary FA composition can influence the gut health and function in pigs and may support a normal immune system and modulate resistance to infectious diseases during especially stressful phases of a pig's life such as post-weaning.

[26] *Lv Q, Wang Y, Li Y et al.* **Rosuvastatin reverses hypertension-induced changes in the aorta structure and endothelium-dependent relaxation in rats through suppression of apoptosis and inflammation**. Journal of cardiovascular pharmacology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32205566
ABSTRACT
Vascular remodeling is one of the most critical complications caused by hypertension. Previous studies have demonstrated that rosuvastatin has anti-inflammatory, antioxidant and antiplatelet effects and therefore can be used to treat cardiovascular disease. In this study, we explored the beneficial effects of rosuvastatin in reversing aortic remodeling in spontaneously hypertensive rats (SHR). After treating with different doses of rosuvastatin, its anti-lipid, anti-apoptosis and anti-

inflammatory effects were determined. We also examined if rosuvastatin can improve the structure and function of the aorta. We found that rosuvastatin treatment of SHRs for two months at two different doses can effectively reduce the media thickness of the aorta compared with the control group. Similarly, rosuvastatin improved the vascular relaxation function of the aortic rings at a high level of acetylcholine in vitro. Mechanistically, it was found that rosuvastatin increased the expression of eNOS and plasma nitrite/nitrate levels. Besides, rosuvastatin suppressed the apoptosis and inflammation and up-regulated the expression of gap-junction complex connexin 43 both in media and endothelium. Lastly, rosuvastatin inhibited the AT1R/PKCalpha/HSP70 signaling transduction pathway. In summary, these findings demonstrated that rosuvastatin could improve the vascular structure and function mainly by increasing eNOS expression and preventing apoptosis and inflammation. This study provided evidence that rosuvastatin has beneficial effects in reversing the remodeling of the aorta due to hypertension.

[27] *Dufour J, Hassan M, Netchiporouk E, Litvinov IV*. **Recent Advances in Evaluating Impact of Biologic Therapy for Moderate-Severe Psoriasis on Cardiovascular Events and Atherosclerotic Plaque Formation**. Journal of cutaneous medicine and surgery 2020; 24:209-210.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32208025
ABSTRACT

[28] *Corpechot C, Rousseau A, Chazouilleres O*. **Switching vs. add-on strategy in PBC treatment: Lessons from UDCA and bezafibrate experience**. Journal of hepatology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32199670
ABSTRACT

[29] *Sugizaki Y, Otake H, Kawamori H et al.* **Adding Alirocumab to Rosuvastatin Helps Reduce the Vulnerability of Thin-Cap Fibroatheroma: An ALTAIR Trial Report**. JACC. Cardiovascular imaging 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32199850
ABSTRACT

[30] *Bayram E, Marras C, Standaert DG et al.* **Progressive Supranuclear Palsy and Statin Use**. Mov Disord 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32220093
ABSTRACT
INTRODUCTION: Statins were proposed to be neuroprotective; however, the effects are unknown in progressive supranuclear palsy (PSP), a pure tauopathy. METHODS: Data of 284 PSP cases and 284 age-matched, sex-matched, and race-matched controls were obtained from the environmental and genetic PSP (ENGENE-PSP) study. Cases were evaluated with the PSP Rating Scale, Unified Parkinson's Disease Rating Scale, Mattis Dementia Rating Scale, and Neuropsychiatric Inventory. Statin associations with PSP risk, onset age, and disease features were analyzed. RESULTS: Univariate models showed lower PSP risk for type 1 statin users (simvastatin, lovastatin, pravastatin). After adjusting for confounding variables, statin use and lower PSP risk association remained only at a trend level. For PSP cases, type 1 statins were associated with 1-year older onset age; type 2 statins (atorvastatin, rosuvastatin) were associated with the lower PSP Rating

Scale and Unified Parkinson's Disease Rating Scale. CONCLUSION: Statins may have inverse associations with PSP risk and motor impairment. Randomized prospective studies are required to confirm this effect. (c) 2020 International Parkinson and Movement Disorder Society.

[31] *Liu Q, Xia H, Zhou S et al.* **Simvastatin Inhibits the Malignant Behaviors of Gastric Cancer Cells by Simultaneously Suppressing YAP and beta-Catenin Signaling**. OncoTargets and therapy 2020; 13:2057-2066.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32210573
ABSTRACT
Background: Statins, which are used to lower blood cholesterol levels by inhibiting HMG-CoA reductase, have shown anticancer effects in many cancer cells. However, the role of statins in gastric cancer remains unclear. This study aims to investigate whether the statins could antagonize progression of gastric cancer cells and tried to find the molecule mechanism. Methods: Effects of simvastatin on the morphology, proliferation, migration, apoptosis, and invasion of gastric cancer cells were detected and compared. Western blotting, cell viability assay, fluorescence, and transfection were employed to study the molecule mechanism of the effects and the interaction between YAP and beta-catenin signaling. Results: Simvastatin could inhibit proliferation, migration and invasion, and promote the apoptosis in gastric cancer cells. Mechanistic studies showed that simvastatin treatment could inhibit the expression of beta-catenin and the activity of YAP and the downstream targets of YAP and beta-catenin in gastric cancer cells. Moreover, we found that YAP and beta-catenin could form a positive feedback loop in gastric cancer cells. Further investigation revealed that simvastatin mainly acted through by inhibiting the activity of RhoA to inhibit YAP and beta-catenin, and the geranylgeranyl pyrophosphate pathway mediated this regulation. Conclusion: Statins represent a promising therapeutic option for gastric cancer by simultaneously targeting YAP and beta-catenin signaling.

[32] *Heise CW, Gallo T, Curry SC, Woosley RL*. **Identification of populations likely to benefit from pharmacogenomic testing**. Pharmacogenetics and genomics 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32209836
ABSTRACT
OBJECTIVES: Pharmacogenomic testing (PGX) implementation is rapidly expanding, including pre-emptive testing funded by health systems. PGX continues to develop an evidence base that it saves money and improves clinical outcomes. Identifying the potential impact of pre-emptive testing in specific populations may aid in the development of a business case. METHODS: We utilized a software tool that can evaluate patient drug lists and identified groups of patients most likely to benefit from implementation of a PGX testing program in a major medical system population. RESULTS: Medication lists were obtained for sixteen patient groups with a total of 82 613 patients. The percent of patients in each group with testing 'Recommended', 'Strongly recommended', or 'Required' ranged from 12.7% in the outpatient pediatric psychiatry group to 75.7% in the any adult inpatient age >50 years group. Some of the highest yield drugs identified were citalopram, simvastatin, escitalopram, metoprolol, clopidogrel, tramadol, and ondansetron. CONCLUSION: We demonstrate a significant number of patients in each group may have benefit, but targeting certain ones for pre-emptive testing may result in the initial highest yield for a health system.

Literature update week 13 (2020)

[33] *Sato S, Akamine Y, Kagaya H et al.* **Changes in PCSK9 and LDL cholesterol concentrations by everolimus treatment and their effects on polymorphisms in PCSK9 and mTORC1**. Pharmacological reports : PR 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32215854
ABSTRACT
BACKGROUND: The purpose of this study was to evaluate the effects of concentrations of proprotein convertase subtilisin/kexin type 9 (PCSK9) and low-density lipoprotein (LDL) cholesterol by the mammalian target of rapamycin (mTOR) inhibitor everolimus and their effects on genetic polymorphisms in the PCSK9 and mTORC1 genes in 53 renal transplant recipients. METHODS: Prior to and on day 15 after everolimus administration, the concentrations of everolimus in blood and PCSK9 and LDL cholesterol in plasma were evaluated. Additionally, mTORC1 (rs2536T>C and rs2295080T>G) and PCSK9 (rs505151G>A, rs562556G>A, and rs11593680C>T) polymorphisms were analyzed. RESULTS: Mean PCSK9 plasma concentrations on day 15 after everolimus treatment were significantly higher than those before treatment (295 versus 214 ng/mL, respectively; p = 0.004). Significant correlations between the area under the blood concentration-time curves (AUC)0-12 on day 15 of everolimus treatment and the change rate in PCSK9 concentrations were found (r = 0.316, p = 0.021). However, there were no significant correlations between the change rate in PCSK9 and LDL cholesterol concentrations. The change rate in PCSK9 concentrations by everolimus treatment was significantly greater in patients with the mTORC1 rs2295080G allele than the T/T genotype (p = 0.006); however, there were no significant differences between PCSK9 rs505151G>A and rs11583680C>T genotypes. In multivariate analyses, patients with mTORC1 rs2295080G (p = 0.010), higher everolimus AUC0-12 (p = 0.006), and female sex (p = 0.029) showed higher change rates of PCSK9 following everolimus therapy. CONCLUSIONS: Administration of everolimus significantly elevated plasma PCSK9 concentrations, potentially causing everolimus-induced hyperlipidemia.

[34] *Kara ZP, Ozturk D, Ozturk N et al.* **Effects of atorvastatin on talinolol absorption: A potential drug-drug interaction**. Pharmazie 2020; 75:70-74.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32213237
ABSTRACT
In this study, we aimed to determine the drug-drug interaction potential between atorvastatin (ATOR), and talinolol (TAL). Concentration-dependent effects of ATOR on the intestinal permeability of TAL were investigated by an in situ intestinal perfusion method. Dose-dependent effects of ATOR on TAL exposure were evaluated by measuring plasma concentrations after oral administration in rats. ATOR slightly changed the intestinal secretion of TAL in jejunum but not in colon. Plasma AUC levels of TAL were elevated by co-administration of ATOR at low and high doses whereas medium doses of ATOR resulted in a decrease in TAL bioavailability. However, these changes were not statistically significant. In our study, the pharmacokinetics of TAL were not affected by the concurrent use of ATOR in rats. In conclusion, it should be considered that complex interplay between the efflux and uptake transporters in the tissues and inhibition of these transporters by modulating agents may overshadow individual effects of each other.

[35] *Zhao C, Hu Y, Chen H et al.* **An in vitro evaluation of the effects of different statins on the structure and function of human gut bacterial community**. PloS one 2020; 15:e0230200.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32214324

ABSTRACT

Statins, a class of drugs that can effectively remove cholesterol from serum, are used to regulate plasma total cholesterol and reduce the risk of cardiovascular diseases, but it is still unclear whether the drug are modulated by gut microbiota or the structures of gut microbiota are shaped by statins. We investigated the interactions between statins and the human gut microbiota during the in vitro fermentation process by 16S rRNA gene sequencing, gas chromatography (GC), and high-performance liquid chromatography (HPLC) analyses. The presence of fluvastatin (FLU2) specifically promoted the growth of Escherichia/Shigella, Ruminococcaceae UCG 014, and Sutterella. However, the composition of the gut bacterial microbiota remained relatively static in samples treated with rosuvastatin (ROS), simvastatin (SIM), and atorvastatin (ATO). The PICRUSt program predicted moderate differences in the functional categories related to the biosynthesis of other secondary metabolites, cellular processes and signaling, and signal transduction in the FLU2 fermentation samples. Our study revealed substantial variation in the structure and function of microbiomes from the FLU2-treated samples. In addition, short-chain fatty acids (SCFAs) were also significantly decreased in FLU2-treated samples compared with the samples treated with other stains. Statins can be degraded by the human gut microbiota in vitro, and the degradation rate was approximately 7%-30% and 19%-48% after fermentation was allowed to proceed for 24 h and 48 h, respectively. Generally, FLU2 could largely shape the composition and function of human gut microbiota, which resulted in changes in the production of SCFAs. In turn, all statins could be degraded or modified by the gut microbiota. Our study paves the way for elucidating statin-gut microbiota interactions in vitro towards the improvement of the host health and personalized medicine.

[36] *Mallah SI, Atallah B, Moustafa F et al.* **Evidence-based pharmacotherapy for prevention and management of cardiac allograft vasculopathy**. Prog Cardiovasc Dis 2020.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32205133

ABSTRACT

Cardiac allograft vasculopathy (CAV)-mediated by a heterogeneous myriad of immune and non-immune factors, which contribute to the progressive and diffuse thickening of the arterial allograft's tunica intima in one distinct form of CAV, and the build-up of plaque in another-is a major limiting factor of long-term survival post heart transplantation. Information on the optimal pharmacotherapeutic approaches for the prevention and management of CAV is conflicting, scattered, and inconsistent, with numerous recent studies adding to the literature. In this paper, we present a go-to clinical resource with the most updated and comprehensive information on the topic. Immunosuppressant therapy remains a staple, with mTOR inhibitors and mycophenolate mofetil (MMF) showing direct correlation with CAV prevention. More data is now available with calcineurin inhibitor (CNI) minimizing or sparing regimens. More novel approaches are being investigated for the roles of monoclonal antibodies, anti-thymocyte globulin, and bortezomib in preventing or delaying CAV. On the other hand, statins' established efficacy is attributed to lipid-lowering and lipid-independent immunomodulatory effects, with early initiation associated with improved outcomes. The choice of statin is dependent on drug-drug interactions. Other aiding approaches for the prevention of CAV include antioxidant vitamins, aspirin, vasodilators, folate therapy, and, most pertinently, cytomegalovirus prophylaxis. Larger clinical trials are needed

before these options are institutionalised. For management of established CAV, early initiation of augmented immunosuppressive therapies may be effective, as well as CNI conversion to mTOR inhibitors with or without standard MMF and azathioprine therapy. Risk of acute rejection needs to be monitored during conversion. Finally, preclinical investigations highlight novel potential therapies for CAV prevention and attenuation, however robust clinical trials are needed to test their efficacy and safety.

[37] *Perez de Isla L, Arroyo-Olivares R, Alonso R et al.* **Incidence of cardiovascular events and changes in the estimated risk and treatment of familial hypercholesterolemia: the SAFEHEART registry**. Revista espanola de cardiologia (English ed.) 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32201274
ABSTRACT
INTRODUCTION AND OBJECTIVES: The SAFEHEART study was designed to analyze the situation of familial heterozygous hypercholesterolemia (FHH) and improve knowledge of this disease in Spain. Our objective was to determine the incidence rate of cardiovascular events, the estimated risk of developing an event and its modification, the use of lipid-lowering treatment, and the achievement of low-density lipoprotein cholesterol targets in patients with FHH. METHODS: SAFEHEART is a prospective, open, multicenter, nationwide cohort study, with long-term protocol-based follow-up in a population of individuals with molecularly-characterized FHH. We analyzed patients older than 18 years with complete follow-up. RESULTS: We included 2648 patients with FHH. The median follow-up was 6.6 (4.8-9.7) years. The overall incidence rate of cardiovascular events was 1.3 events/100 patient-years. After the follow-up, the 10-year estimated risk of developing a cardiovascular event was reduced from 1.6% to 1.3% (P <.001). In the last follow-up, 20.6% and 22.2% of the patients in primary and secondary prevention achieved low-density lipoprotein cholesterol values <100mg/dL and <70mg/dL, respectively. CONCLUSIONS: This study was performed in the largest population of patients with FHH in Spain. We identified the incidence rate of cardiovascular events, the estimated risk of developing a cardiovascular event and its modification, the achievement of low-density lipoprotein cholesterol targets, and the therapeutic management in this population. Although the cardiovascular risk of FHH is high, appropriate treatment reduces the likelihood of an event. CLINICAL TRIAL REGISTRATION: http://www.clinicaltrials.gov. Identifier: NCT02693548.

[38] *Pralong F, Gojanovic B*. **[Physical activity : under-used therapeutic option in the treatment of metabolic diseases]**. Revue medicale suisse 2020; 16:578-581.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32216180
ABSTRACT
It is well demonstrated that physical activity can improve the control of diseases such as diabetes, or dyslipidemia. Introduction of regular and frequent physical activity is also part of the useful measures in the management of excess weight. It is therefore surprising that the prescription of physical activity for the treatment of these diseases is still not part of the curriculum of medical studies, and that reimbursement remains very scarce. This article summarizes the state of scientific knowledge in the field and outlines their clinical application.

[39] *Kummen M, Solberg OG, Storm-Larsen C et al.* **Rosuvastatin alters the genetic composition of the human gut microbiome**. Scientific reports 2020; 10:5397.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32214138
ABSTRACT
The gut microbiome contributes to the variation of blood lipid levels, and secondary bile acids are associated with the effect of statins. Yet, our knowledge of how statins, one of our most common drug groups, affect the human microbiome is scarce. We aimed to characterize the effect of rosuvastatin on gut microbiome composition and inferred genetic content in stool samples from a randomized controlled trial (n = 66). No taxa were significantly altered by rosuvastatin during the study. However, rosuvastatin-treated participants showed a reduction in the collective genetic potential to transport and metabolize precursors of the pro-atherogenic metabolite trimethylamine-N-oxide (TMAO, $p < 0.01$), and an increase of related metabolites betaine and gamma-butyrobetaine in plasma ($p < 0.01$). Exploratory analyses in the rosuvastatin group showed that participants with the least favorable treatment response (defined as < median change in high-density/low-density lipoprotein (HDL/LDL) ratio) showed a marked increase in TMAO-levels compared to those with a more favorable response ($p < 0.05$). Our data suggest that while rosuvastatin has a limited effect on gut microbiome composition, it could exert broader collective effects on the microbiome relevant to their function, providing a rationale for further studies of the influence of statins on the gut microbiome.

[40] *Xu Z, Li M, Lyu J et al.* **Different risk factors in identical features of intracranial atherosclerosis plaques in the posterior and anterior circulation in high-resolution MRI**. Ther Adv Neurol Disord 2020; 13:1756286420909991.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32206091
ABSTRACT
Background: We constructed a high-volume registry to identify whether risk factors of intracranial atherosclerotic plaque (ICAP) features differ in the posterior and anterior circulation in patients with symptomatic intracranial atherosclerotic stenosis (ICAS) investigated by high-resolution magnetic resonance imaging (HRMRI). Methods: The registry was constructed for patients with symptomatic ICAS who underwent HRMRI for culprit plaques. ICAP-vulnerable features included positive remodelling, diffuse distribution, intraplaque haemorrhage and strong enhancement. Results: We analysed risk factors for the same ICAP features between the posterior and anterior circulation in data of 97 patients in the posterior circulation and 105 patients in the anterior circulation ICAPs. In patients with diffuse distribution, the probability of being female were lower [odds ratio (OR):0.08; 95% confidence interval (CI):0.02-0.34; $p = 0.001$] and having diabetes mellitus was higher (OR: 7.75; 95% CI:1.75-34.39; $p = 0.007$) in posterior circulation patients. In patients with strong enhancement, the probability of having diabetes was higher in posterior circulation patients (OR:6.71; 95% CI:1.37-32.81; $p = 0.019$). Conclusions: Our results demonstrate more risk factors in the posterior than in the anterior circulation in patients with the same ICAP-vulnerable features, highlighting the need for stratification of risk factors in symptomatic ICAPs. Trial Registration: URL: http://www.clinicaltrials.gov. Unique identifier: NCT02705599.