[1] *Torrandell-Haro G, Branigan GL, Vitali F et al.* **Statin therapy and risk of Alzheimer's and age-related neurodegenerative diseases**. Alzheimers Dement (N Y) 2020; 6:e12108.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33283039

ABSTRACT

INTRODUCTION: Establishing efficacy of and molecular pathways for statins has the potential to impact incidence of Alzheimer's and age-related neurodegenerative diseases (NDD). METHODS: This retrospective cohort study surveyed US-based Humana claims, which includes prescription and patient records from private-payer and Medicare insurance. Claims from 288,515 patients, aged 45 years and older, without prior history of NDD or neurological surgery, were surveyed for a diagnosis of NDD starting 1 year following statin exposure. Patients were required to be enrolled with claims data for at least 6 months prior to first statin prescription and at least 3 years thereafter. Computational system biology analysis was conducted to determine unique target engagement for each statin. RESULTS: Of the 288,515 participants included in the study, 144,214 patients (mean [standard deviation (SD)] age, 67.22 [3.8] years) exposed to statin therapies, and 144,301 patients (65.97 [3.2] years) were not treated with statins. The mean (SD) follow-up time was 5.1 (2.3) years. Exposure to statins was associated with a lower incidence of Alzheimer's disease (1.10% vs 2.37%; relative risk [RR], 0.4643; 95% confidence interval [CI], 0.44-0.49; P < .001), dementia 3.03% vs 5.39%; RR, 0.56; 95% CI, 0.54-0.58; P < .001), multiple sclerosis (0.08% vs 0.15%; RR, 0.52; 95% CI, 0.41-0.66; P < .001), Parkinson's disease (0.48% vs 0.92%; RR, 0.53; 95% CI, 0.48-0.58; P < .001), and amyotrophic lateral sclerosis (0.02% vs 0.05%; RR, 0.46; 95% CI, 0.30-0.69; P < .001). All NDD incidence for all statins, except for fluvastatin (RR, 0.91; 95% CI, 0.65-1.30; P = 0.71), was reduced with variances in individual risk profiles. Pathway analysis indicated unique and common profiles associated with risk reduction efficacy. DISCUSSION: Benefits and risks of statins relative to neurological outcomes should be considered when prescribed for at-risk NDD populations. Common statin activated pathways indicate overarching systems required for risk reduction whereas unique targets could advance a precision medicine approach to prevent neurodegenerative diseases.

[2] *Kaneko H, Itoh H, Kiriyama H et al.* **Lipid Profile and Subsequent Cardiovascular Disease among Young Adults Aged < 50 Years**. The American journal of cardiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33301771

ABSTRACT

Epidemiological evidence on the relationship between lipid profile and cardiovascular disease (CVD) events in young adults remains insufficient. Thus, we sought to explore the association of lipid profile with subsequent CVD among young adults. Medical records of 1,451,997 young adults (20 to 49 years old) without prior history of CVD and not taking lipid lowering medications were extracted from the Japan Medical Data Center, a nationwide epidemiological database. We conducted multivariable Cox regression analyses to identify the association between lipid profile and the subsequent risk of CVD and used multiple imputation for missing data on body mass index, waist circumference, hypertension, diabetes mellitus, and cigarette smoking in our database. The mean age was 39.0 ± 7.4 years, and 58.5% were men. After a mean follow-up of 1,148 ± 893 days, myocardial infarction, angina pectoris, stroke, and heart failure developed in 1,638 (0.1%), 15,887 (1.1%), 5,593 (0.4%), and 14,351 (1.0%) subjects, respectively. Multivariable Cox regression analyses including covariates after multiple imputation for missing values demonstrated that LDL-C ≥ 140 mg/dL, HDL-C < 40

mg/dL, and triglycerides ≥ 150 mg/dL were independently associated with the incidence of myocardial infarction, angina pectoris, and heart failure. However, they were not associated with the incidence of stroke. Multivariable Cox regression analyses including the number of abnormal lipid profiles and covariates showed that the incidence of myocardial infarction, angina, and heart failure increased stepwise with the number of abnormal lipid profiles. However, the number of abnormal lipid profiles was not associated with the subsequent risk of stroke. In conclusion, the comprehensive analysis of a nationwide epidemiological database demonstrated a close relationship between lipid profile and subsequent CVD, suggesting the importance of maintaining an optimal lipid profile for the primary prevention of CVD in young generations.

[3] *Lim GJ, Liu YL, Low S et al.* **Medical Costs Associated with Severity of Chronic Kidney Disease in Type 2 Diabetes Mellitus in Singapore**. Ann Acad Med Singap 2020; 49:731-741.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33283836

ABSTRACT

INTRODUCTION: This was a retrospective cross-sectional study to assess the impact of chronic kidney disease (CKD) and its severity in Type 2 diabetes mellitus (T2DM) on direct medical costs, and the effects of economic burden on CKD related complications in T2DM in Singapore. METHODS: A total of 1,275 T2DM patients were recruited by the diabetes centre at Khoo Teck Puat Hospital from 2011-2014. CKD stages were classified based on improving global outcome (KDIGO) categories, namely the estimated glomerular filtration rate (eGFR) and albuminuria kidney disease. Medical costs were extracted from the hospital administrative database. RESULTS: CKD occurred in 57.3% of patients. The total mean cost ratio for CKD relative to non-CKD was 2.2 (P<0.001). Mean (median) baseline annual unadjusted costs were significantly higher with increasing CKD severity-S$1,523 (S$949), S$2,065 (S$1,198), S$3,502 (S$1,613), and S$5,328 (S$2,556) for low, moderate, high, and very high risk respectively (P<0.001). CKD (P<0.001), age at study entry (P=0.001), Malay ethnicity (P=0.035), duration of diabetes mellitus (DM; P<0.001), use of statins/fibrates (P=0.021), and modified Diabetes Complications Severity Index (DCSI) (P<0.001) were positively associated with mean annual direct medical costs in the univariate analysis. In the fully adjusted model, association with mean annual total costs persisted for CKD, CKD severity and modified DCSI. CONCLUSION: The presence and increased severity of CKD is significantly associated with higher direct medical costs in T2DM patients. Actively preventing the occurrence and progression in DM-induced CKD may significantly reduce healthcare resource consumption and healthcare costs.

[4] *Guo Y, Yan B, Tai S et al.* **PCSK9: Associated with cardiac diseases and their risk factors?** Archives of biochemistry and biophysics 2020:108717.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33307067

ABSTRACT

PCSK9 plays a critical role in cholesterol metabolism via the PCSK9-LDLR axis. Liver-derived, circulating PCSK9 has become a novel drug target in lipid-lowering therapy. Accumulative evidence supports the possible association between PCSK9 and cardiac diseases and their risk factors. PCSK9 exerts various effects in the heart independently of LDL-cholesterol regulation. Acute myocardial infarction (AMI) induces local and systemic inflammation and reactive oxygen species generation, resulting in increased PCSK9 expression in hepatocytes and cardiomyocytes. PCSK9 upregulation promotes excessive autophagy and apoptosis in cardiomyocytes, thereby contributing to

cardiac insufficiency. PCSK9 might also participate in the pathophysiology of heart failure by regulating fatty acid metabolism and cardiomyocyte contractility. It also promotes platelet activation and coagulation in patients with atrial fibrillation. PCSK9 is an independent predictor of aortic valve calcification and accelerates calcific aortic valve disease by regulating lipoprotein(a) catabolism. Accordingly, the use of PCSK9 inhibitors significantly reduced infarct sizes and arrhythmia and improves cardiac contractile function in a rat model of AMI. Circulating PCSK9 levels are positively correlated with age, diabetes mellitus, obesity, and hypertension. Here, we reviewed recent clinical and experimental studies exploring the association between PCSK9, cardiac diseases, and their related risk factors and aiming to identify possible underlying mechanisms.

[5] *Haberal İ, Yesiltas MA, Koyuncu AO et al.* **Is it possible to predict atherosclerosis in the ascending aorta by the patient's lipid panel?** Archives of medical sciences. Atherosclerotic diseases 2020; 5:e237-e244.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33305062
ABSTRACT
INTRODUCTION: Atherosclerosis is a chronic inflammatory event characterized by stiffness and thickening of the vascular walls. In our daily practice, we assume the atherosclerotic potential of the patient by following the total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL) and triglyceride levels (lipid panel). We aimed to understand the relation between the HDL, LDL, cholesterol levels and the atherosclerosis in large vascular structures such as the ascending aorta. MATERIAL AND METHODS: We have searched for atherosclerosis in the aortic tissue samples from 48 patients. It is a study in which we examine the correlation of preoperative cholesterol values (HDL, LDL, triglyceride, total cholesterol) by dividing the patients into two groups according to the presence of plaque. RESULTS: Forty-three (89.6%) male and 5 (10.4%) female patients between 39 and 81 years of age were included in the study. There was no statistically significant difference between the patients' preoperative cardiovascular risk assessments. The free T3 values were within the normal range in all patients, but there was a difference that patients in the non-atherosclerosis group had lower values. There was no statistically significant difference between the two groups' HDL, LDL, total cholesterol, or triglyceride parameters. CONCLUSIONS: As a result, in our study, no significant difference was found between HDL-C, LDL-C, triglyceride, total cholesterol values and the pathological process of aortic atherosclerosis. As a result of this study, we believe that it was necessary to correct the error margins of these parameters. In addition, it required the need for a clearer laboratory parameter to demonstrate atherosclerosis.

[6] *Cesena FHY*. **Lifestyle in the Very Elderly Matters**. Arquivos brasileiros de cardiologia 2020; 115:882-884.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33295450
ABSTRACT

[7] *Heffron SP, Ruuth MK, Xia Y et al.* **Low-density lipoprotein aggregation predicts adverse cardiovascular events in peripheral artery disease**. Atherosclerosis 2021; 316:53-57.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33307457
ABSTRACT

BACKGROUND AND AIMS: Peripheral artery disease (PAD) is a systemic manifestation of atherosclerosis that is associated with a high risk of major adverse cardiovascular events (MACE). LDL aggregation contributes to atherosclerotic plaque progression and may contribute to plaque instability. We aimed to determine if LDL aggregation is associated with MACE in patients with PAD undergoing lower extremity revascularization (LER). METHODS: Two hundred thirty-nine patients with PAD undergoing LER had blood collected at baseline and were followed prospectively for MACE (myocardial infarction, stroke, cardiovascular death) for one year. Nineteen age, sex and LDL-C-matched control subjects without cardiovascular disease also had blood drawn. Subject LDL was exposed to sphingomyelinase and LDL aggregate size measured via dynamic light scattering. RESULTS: Mean age was 72.3 ± 10.9 years, 32.6% were female, and LDL-cholesterol was 68 ± 25 mg/dL. LDL aggregation was inversely associated with triglycerides, but not associated with demographics, LDL-cholesterol or other risk factors. Maximal LDL aggregation occurred significantly earlier in subjects with PAD than in control subjects. 15.9% of subjects experienced MACE over one year. The 1st tertile (shortest time to maximal aggregation) exhibited significantly higher MACE (25% vs. 12.5% in tertile 2 and 10.1% in tertile 3, p = 0.012). After multivariable adjustment for demographics and CVD risk factors, the hazard ratio for MACE in the 1st tertile was 4.57 (95% CI 1.60-13.01; p = 0.004) compared to tertile 3. Inclusion of LDL aggregation in the Framingham Heart Study risk calculator for recurrent coronary heart disease events improved the c-index from 0.57 to 0.63 (p = 0.01). CONCLUSIONS: We show that in the setting of very well controlled LDL-cholesterol, patients with PAD with the most rapid LDL aggregation had a significantly elevated MACE risk following LER even after multivariable adjustment. This measure further improved the classification specificity of an established risk prediction tool. Our findings support broader investigation of this assay for risk stratification in patients with atherosclerotic CVD.

[8] *Kheirkhah A, Lamina C, Rantner B et al.* **Elevated levels of serum PCSK9 in male patients with symptomatic peripheral artery disease: The CAVASIC study**. Atherosclerosis 2021; 316:41-47. **PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33302043

ABSTRACT

BACKGROUND AND AIMS: Peripheral artery disease (PAD) affects more than 200 million people worldwide. Increased low-density lipoprotein cholesterol (LDL-C)levels are a risk factor for PAD and the concentrations are influenced by proprotein convertase subtilisin/kexin type 9 (PCSK9). PCSK9 regulates the recycling of the LDL receptors to the cell membrane surface. Only a limited number of mostly small studies investigated the association between serum PCSK9 concentrations and PAD of different definition, which revealed contrasting results. METHODS: Serum PCSK9, lipoprotein(a) [Lp(a)] and other lipoprotein concentrations were measured in male participants of the CAVASIC study, a case-control study of 248 patients with intermittent claudication and 251 age and diabetes-matched controls. RESULTS: PAD patients had significantly higher PCSK9 concentrations when compared to controls (250 ± 77 vs. 222 ± 68 ng/mL, p < 0.001). Logistic regression analysis with adjustment for age revealed that an increase in PCSK9 concentrations of 100 ng/mL was associated with a 1.78-fold higher risk for PAD (95%CI 1.38-2.33, p = 1.43 × 10(-5)). The association attenuated, but was still significant when adjusting additionally for age, Lp(a)-corrected LDL cholesterol, HDL cholesterol, high-sensitivity-CRP, statin treatment, hypertension, diabetes mellitus and smoking (OR = 1.49, 95%CI 1.03-2.18, p = 0.035). The strongest association was observed when both PCSK9 concentrations were above the median and Lp(a) concentrations were above 30 mg/dL (OR = 3.35,

95%CI 1.49-7.71, p = 0.0038). CONCLUSIONS: Our findings suggest an association of higher PCSK9 concentrations with PAD, which was independent of other lipid parameters and classical cardiovascular risk factors.

[9] *So J, Wu D, Lichtenstein AH et al.* **EPA and DHA differentially modulate monocyte inflammatory response in subjects with chronic inflammation in part via plasma specialized pro-resolving lipid mediators: A randomized, double-blind, crossover study**. Atherosclerosis 2021; 316:90-98.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33303222
ABSTRACT
BACKGROUND AND AIMS: The independent effects of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) on chronic inflammation through their downstream lipid mediators, including the specialized pro-resolving lipid mediators (SPM), remain unstudied. Therefore, we compared the effects of EPA and DHA supplementation on monocyte inflammatory response and plasma polyunsaturated fatty acids (PUFA) SPM lipidome. METHODS: After a 4-week lead-in phase (baseline), 9 men and 12 postmenopausal women (50-75 years) with chronic inflammation received two phases of 10-week supplementation with 3 g/day EPA and DHA in a random order, separated by a 10-week washout. RESULTS: Compared with baseline, EPA and DHA supplementation differently modulated LPS-stimulated monocyte cytokine expression. EPA lowered TNFA ($p < 0.001$) whereas DHA reduced TNFA ($p < 0.001$), IL6 ($p < 0.02$), MCP1 ($p < 0.03$), and IL10 ($p < 0.01$). DHA lowered IL10 expression relative to EPA ($p = 0.03$). Relative to baseline, EPA, but not DHA, decreased the ratios of TNFA/IL10 and MCP1/IL10 (both $p < 0.01$). EPA and DHA also significantly changed plasma PUFA SPM lipidome by replacing n-6 AA derivatives with their respective derivatives including 18-hydroxy-EPA (+5 fold by EPA) and 17- and 14-hydroxy-DHA (+3 folds by DHA). However, DHA showed a wider effect than EPA by also significantly increasing EPA derivatives and DPA-derived SPM at a greater expense of AA derivatives. Different groups of PUFA derivatives mediated the differential effects of EPA and DHA on monocyte cytokine expression. CONCLUSIONS: EPA and DHA had distinct effects on monocyte inflammatory response with a broader effect of DHA in attenuating pro-inflammatory cytokines. These differential effects were potentially mediated by different groups of PUFA derivatives, suggesting immunomodulatory activities of SPM and their intermediates.

[10] *Härdtner C, Kornemann J, Krebs K et al.* **Inhibition of macrophage proliferation dominates plaque regression in response to cholesterol lowering**. Basic research in cardiology 2020; 115:78.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33296022
ABSTRACT
Statins induce plaque regression characterized by reduced macrophage content in humans, but the underlying mechanisms remain speculative. Studying the translational APOE*3-Leiden.CETP mouse model with a humanized lipoprotein metabolism, we find that systemic cholesterol lowering by oral atorvastatin or dietary restriction inhibits monocyte infiltration, and reverses macrophage accumulation in atherosclerotic plaques. Contrary to current believes, none of (1) reduced monocyte influx (studied by cell fate mapping in thorax-shielded irradiation bone marrow chimeras), (2) enhanced macrophage egress (studied by fluorescent bead labeling and transfer), or (3) atorvastatin

accumulation in murine or human plaque (assessed by mass spectrometry) could adequately account for the observed loss in macrophage content in plaques that undergo phenotypic regression. Instead, suppression of local proliferation of macrophages dominates phenotypic plaque regression in response to cholesterol lowering: the lower the levels of serum LDL-cholesterol and lipid contents in murine aortic and human carotid artery plaques, the lower the rates of in situ macrophage proliferation. Our study identifies macrophage proliferation as the predominant turnover determinant and an attractive target for inducing plaque regression.

[11] *Demopoulos C, Antonopoulou S, Theoharides TC*. **COVID-19, microthromboses, inflammation, and platelet activating factor**. Biofactors 2020; 46:927-933.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33296106
ABSTRACT
Recent articles report elevated markers of coagulation, endothelial injury, and microthromboses in lungs from deceased COVID-19 patients. However, there has been no discussion of what may induce intravascular coagulation. Platelets are critical in the formation of thrombi and their most potent trigger is platelet activating factor (PAF), first characterized by Demopoulos and colleagues in 1979. PAF is produced by cells involved in host defense and its biological actions bear similarities with COVID-19 disease manifestations. PAF can also stimulate perivascular mast cell activation, leading to inflammation implicated in severe acute respiratory syndrome (SARS). Mast cells are plentiful in the lungs and are a rich source of PAF and of inflammatory cytokines, such as IL-1β and IL-6, which may contribute to COVID-19 and especially SARS. The histamine-1 receptor antagonist rupatadine was developed to have anti-PAF activity, and also inhibits activation of human mast cells in response to PAF. Rupatadine could be repurposed for COVID-19 prophylaxis alone or together with other PAF-inhibitors of natural origin such as the flavonoids quercetin and luteolin, which have antiviral, anti-inflammatory, and anti-PAF actions.

[12] *Udani SD, Bhogal P*. **Black blood vessel wall MRI to identify vulnerable atherosclerotic plaque in a non-stenotic intracranial vertebral artery as a cause of acute ischaemia**. BJR Case Rep 2020; 6:20200061.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33299594
ABSTRACT
Conventional neuroimaging techniques for investigating the cause of stroke are mainly centred on investigating luminal stenosis. The pathophysiology of intracranial atherosclerotic disease (ICAD) and stroke is complex and extends beyond just vessel narrowing. The concept of the vulnerable atherosclerotic plaque, that can result in acute coronary syndromes, has been well described in the cardiac literature(1,2)although this concept is less well accepted among stroke physicians. We describe a case of a 61-year-old male with acute neurological sequelae from a non-stenotic atherosclerotic plaque of the intracranial vertebral artery. This case report describes the additional use of vessel wall MRI techniques to aid the radiologist in identifying such vulnerable lesions and therefore helping to tailor management and prevent further clinical deterioration.

[13] *Johannesen CDL, Langsted A, Mortensen MB, Nordestgaard BG*. **Association between low density lipoprotein and all cause and cause specific mortality in Denmark: prospective cohort study**. Bmj 2020; 371:m4266.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33293274

ABSTRACT

OBJECTIVE: To determine the association between levels of low density lipoprotein cholesterol (LDL-C) and all cause mortality, and the concentration of LDL-C associated with the lowest risk of all cause mortality in the general population. DESIGN: Prospective cohort study. SETTING: Denmark; the Copenhagen General Population Study recruited in 2003-15 with a median follow-up of 9.4 years. PARTICIPANTS: Individuals randomly selected from the national Danish Civil Registration System. MAIN OUTCOME MEASURES: Baseline levels of LDL-C associated with risk of mortality were evaluated on a continuous scale (restricted cubic splines) and by a priori defined centile categories with Cox proportional hazards regression models. Main outcome was all cause mortality. Secondary outcomes were cause specific mortality (cardiovascular, cancer, and other mortality). RESULTS: Among 108 243 individuals aged 20-100, 11 376 (10.5%) died during the study, at a median age of 81. The association between levels of LDL-C and the risk of all cause mortality was U shaped, with low and high levels associated with an increased risk of all cause mortality. Compared with individuals with concentrations of LDL-C of 3.4-3.9 mmol/L (132-154 mg/dL; 61st-80th centiles), the multivariable adjusted hazard ratio for all cause mortality was 1.25 (95% confidence interval 1.15 to 1.36) for individuals with LDL-C concentrations of less than 1.8 mmol/L (<70 mg/dL; 1st-5th centiles) and 1.15 (1.05 to 1.27) for LDL-C concentrations of more than 4.8 mmol/L (>189 mg/dL; 96th-100th centiles). The concentration of LDL-C associated with the lowest risk of all cause mortality was 3.6 mmol/L (140 mg/dL) in the overall population and in individuals not receiving lipid lowering treatment, compared with 2.3 mmol/L (89 mg/dL) in individuals receiving lipid lowering treatment. Similar results were seen in men and women, across age groups, and for cancer and other mortality, but not for cardiovascular mortality. Any increase in LDL-C levels was associated with an increased risk of myocardial infarction. CONCLUSIONS: In the general population, low and high levels of LDL-C were associated with an increased risk of all cause mortality, and the lowest risk of all cause mortality was found at an LDL-C concentration of 3.6 mmol/L (140 mg/dL).

[14] *Russell JA, Marshall JC, Slutsky A et al.* **Study protocol for a multicentre, prospective cohort study of the association of angiotensin II type 1 receptor blockers on outcomes of coronavirus infection**. BMJ open 2020; 10:e040768.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33293316

ABSTRACT

INTRODUCTION: The COVID-19 epidemic grows and there are clinical trials of antivirals. There is an opportunity to complement these trials with investigation of angiotensin II type 1 receptor blockers (ARBs) because an ARB (losartan) was effective in murine influenza pneumonia. METHODS AND ANALYSIS: Our innovative design includes: ARBs; alignment with the WHO Ordinal Scale (primary endpoint) to align with other COVID-19 trials; joint longitudinal analysis; and predictive biomarkers (angiotensins I, 1-7, II and ACE1 and ACE2). Our hypothesis is: ARBs decrease the need for hospitalisation, severity (need for ventilation, vasopressors, extracorporeal membrane oxygenation or renal replacement therapy) or mortality of hospitalised COVID-19 infected adults. Our two-pronged multicentre pragmatic observational cohort study examines safety and effectiveness of ARBs in (1) hospitalised adult patients with COVID-19 and (2) out-patients already on or not on ARBs. The primary outcome will be evaluated by ordinal logistic regression and main secondary outcomes by both joint longitudinal modelling analyses. We will compare rates of hospitalisation of ARB-exposed

versus not ARB-exposed patients. We will also determine whether continuing ARBs or not decreases the primary outcome. Based on published COVID-19 cohorts, assuming 15% of patients are ARB-exposed, a total sample size of 497 patients can detect a proportional OR of 0.5 (alpha=0.05, 80% power) comparing WHO scale of ARB-exposed versus non-ARB-exposed patients. ETHICS AND DISSEMINATION: This study has core institution approval (UBC Providence Healthcare Research Ethics Board) and site institution approvals (Health Research Ethics Board, University of Alberta; Comite d'etique de la recerche, CHU Sainte Justine (for McGill University and University of Sherbrook); Conjoint Health Research Ethics Board, University of Calgary; Queen's University Health Sciences & Affiliated Hospitals Research Ethics Board; Research Ethics Board, Sunnybrook Health Sciences Centre; Veritas Independent Research Board (for Humber River Hospital); Mount Sinai Hospital Research Ethics Board; Unity Health Toronto Research Ethics Board, St. Michael's Hospital). Results will be disseminated by peer-review publication and social media releases. TRIAL REGISTRATION NUMBER: NCT04510623.

[15] *El Said NO, El Wakeel LM, Khorshid H et al.* **Impact of lipophilic vs hydrophilic statins on the clinical outcome and biomarkers of remodelling in heart failure patients: A prospective comparative randomized study**. British journal of clinical pharmacology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33294980
ABSTRACT
AIMS: There are insufficient direct comparative studies addressing the impact of the type of statin on their respective efficacy in heart failure (HF). The aim of the current study was to compare the effects of lipophilic (atorvastatin) vs hydrophilic (rosuvastatin) on left ventricular function, inflammatory and fibrosis biomarkers in patients with chronic HF. METHODS: This was a prospective, randomized, comparative, parallel study. A total of 85 patients with chronic HF optimized on guideline directed therapy were randomized to receive either atorvastatin 40 mg (n = 42) or rosuvastatin 20 mg (n = 43) for 6 months. Baseline and follow-up assessment included 2D echocardiography, measurement of N-terminal pro-brain natriuretic peptide, interleukin-6 and soluble suppression of tumorigenicity 2 (sST2) levels, liver enzymes and lipid profile. RESULTS: The increase in left ventricular ejection fraction was significantly higher in the atorvastatin group compared to the rosuvastatin group (6.5% [3-11] vs 4% [2-5], P = .006). The reduction in left ventricular end diastolic and end systolic volume was comparable between the 2 groups. The decrease in sST2 levels in pg/mL was significantly higher in the atorvastatin compared to the rosuvastatin group (-255 [-383 to -109.8 vs - 151 [-216 to -69], P = .003). There was a significant reduction in N-terminal pro-brain natriuretic peptide and interleukin-6 levels in both groups, yet the reduction was comparable in both groups. CONCLUSION: The study results suggest that lipophilic atorvastatin is superior to hydrophilic rosuvastatin in increasing left ventricular ejection fraction and reducing fibrosis marker sST2 in HF patients. Trial registration ID: NCT03255044, registered on 21 August 2017.

[16] *Grande E, Giovannini M, Marriere E et al.* **Effect of capmatinib on the pharmacokinetics of digoxin and rosuvastatin administered as a 2-drug cocktail in patients with MET-dysregulated advanced solid tumours: A phase I, multicentre, open-label, single-sequence drug-drug interaction study**. British journal of clinical pharmacology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33300203
ABSTRACT

AIMS: Capmatinib, an orally bioavailable, highly potent and selective MET inhibitor, was recently approved to treat adult patients with metastatic nonsmall cell lung cancer with METex14 skipping mutations. The study investigated the effect of capmatinib on the pharmacokinetics of a single oral dose of digoxin and rosuvastatin in patients with MET-dysregulated advanced solid tumours. METHODS: This was a multicentre, open-label, single-sequence study. An oral drug cocktail containing 0.25 mg digoxin and 10 mg rosuvastatin was administered to adult patients with MET-dysregulated advanced solid tumours on Day 1, and then on Day 22 with capmatinib. Between Days 11 and 32, capmatinib 400 mg was administered twice daily to ensure the attainment of steady state for drug-drug interaction assessment. Pharmacokinetics of cocktail drugs and safety of capmatinib were evaluated. RESULTS: Thirty-two patients were enrolled. Compared to digoxin alone, the geometric mean ratios (90% confidence interval) of area under the concentration-time curve from time zero to infinity and maximum concentration for digoxin plus capmatinib were 1.47 (1.28, 1.68) and 1.74 (1.43, 2.13), respectively. Compared to rosuvastatin alone, the geometric mean ratios (90% confidence interval) of area under the curve to infinity and maximum concentration for rosuvastatin plus capmatinib were 2.08 (1.56, 2.76) and 3.04 (2.36, 3.92), respectively. Most frequent adverse events (≥25% for all grades) were nausea, asthenia, constipation, vomiting, peripheral oedema and pyrexia. Most frequent Grade 3/4 adverse events (≥5%) were anaemia, pulmonary embolism, asthenia, dyspnoea, nausea and vomiting. CONCLUSION: This study demonstrated that capmatinib is an inhibitor of P-gp and BCRP transporters, with clinically relevant drug-drug interaction potential. Capmatinib was well-tolerated and no unexpected safety concerns were observed.

[17] *Feldt M, Menard J, Rosendahl AH et al.* **The effect of statin treatment on intratumoral cholesterol levels and LDL receptor expression: a window-of-opportunity breast cancer trial**. Cancer & metabolism 2020; 8:25.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33292612
ABSTRACT
BACKGROUND: Deregulated lipid metabolism is common in cancer cells and the mevalonate pathway, which synthesizes cholesterol, is central in lipid metabolism. This study aimed to assess statin-induced changes of the intratumoral levels of cholesterol and the expression of the low-density lipoprotein receptor (LDLR) to enhance our understanding of the role of the mevalonate pathway in cancer cholesterol metabolism. METHODS: This study is based on a phase II clinical trial designed as a window-of-opportunity trial including 50 breast cancer patients treated with 80 mg of atorvastatin/day for 2 weeks, between the time of diagnosis and breast surgery. Lipids were extracted from frozen tumor tissue sampled pre- and post-atorvastatin treatment. Intratumoral cholesterol levels were measured using a fluorometric quantitation assay. LDLR expression was evaluated by immunohistochemistry on formalin-fixed paraffin-embedded tumor tissue. Paired blood samples pre- and post-atorvastatin were analyzed for circulating low-density lipoprotein (LDL), high-density lipoprotein (HDL), apolipoprotein A1, and apolipoprotein B. In vitro experiments on MCF-7 breast cancer cells treated with atorvastatin were performed for comparison on the cellular level. RESULTS: In the trial, 42 patients completed all study parts. From the paired tumor tissue samples, assessment of the cholesterol levels was achievable for 14 tumors, and for the LDLR expression in 24 tumors. Following atorvastatin treatment, the expression of LDLR was significantly increased (P = 0.004), while the intratumoral levels of total cholesterol remained stable. A positive association between intratumoral cholesterol levels and tumor proliferation measured by Ki-67 expression was found. In

agreement with the clinical findings, results from in vitro experiments showed no significant changes of the intracellular cholesterol levels after atorvastatin treatment while increased expression of the LDLR was found, although not reaching statistical significance. CONCLUSIONS: This study shows an upregulation of LDLR and preserved intratumoral cholesterol levels in breast cancer patients treated with statins. Together with previous findings on the anti-proliferative effect of statins in breast cancer, the present data suggest a potential role for LDLR in the statin-induced regulation of breast cancer cell proliferation. TRIAL REGISTRATION: The study has been registered at ClinicalTrials.gov (i.e., ID number: NCT00816244 , NIH), December 30, 2008.

[18] *Shi J, Zhang W, Niu Y et al.* **Association of circulating proprotein convertase subtilisin/kexin type 9 levels and the risk of incident type 2 diabetes in subjects with prediabetes: a population-based cohort study**. Cardiovascular diabetology 2020; 19:209.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33302966

ABSTRACT

BACKGROUND: Proprotein convertase subtilisin/kexin type 9 (PCSK9) regulates cholesterol metabolism by targeting the low-density lipoprotein receptor. Recent studies have shown that circulating PCSK9 is associated with glucose homeostasis and insulin resistance. The aim of this study was to examine the association of circulating PCSK9 levels and risk for the development of type 2 diabetes in individuals with prediabetes. METHODS: A population-based prospective study was conducted among 4205 Chinese subjects with prediabetes (average age 56.1 ± 7.5 years). Incident type 2 diabetes was diagnosed according to 2010 American Diabetes Association criteria. Circulating PCSK9 levels were measured using a commercially available enzyme-linked immunosorbent assay (ELISA). The association of circulating PCSK9 levels with the risk of incident type 2 diabetes was assessed by Cox regression analysis. RESULTS: During a median follow-up period of 3.1 years, 568 subjects developed type 2 diabetes. Baseline circulating PCSK9 levels were significantly higher in female subjects developing incident type 2 diabetes than in those not developing incident type 2 diabetes ($p < 0.001$). In female subjects, the risk of incident type 2 diabetes was significantly higher in the highest PCSK9 quartile group (hazard ratio 2.16; 95% confidence interval 1.16-4.04) than in the lowest quartile group after adjustments for age, body mass index, waist circumference, C-reactive protein, γ-glutamyltransferase, triglycerides, low-density lipoprotein cholesterol, systolic blood pressure, and homeostatic model assessment of insulin resistance score. No significant association was observed between PCSK9 and incident type 2 diabetes in male subjects. CONCLUSION: Elevated circulating PCSK9 levels are associated with an increased incidence of type 2 diabetes in female subjects with prediabetes.

[19] *Cruz Rodriguez JB, Mishra K, Siddiqui T.* **Antithrombotic / Antiplatelet Therapy in Patients with Stable Coronary Artery Disease and after Acute Coronary Syndrome**. Cardiovascular & hematological agents in medicinal chemistry 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33290202

ABSTRACT

The major physiopathological mechanism underlying acute coronary syndromes (ACS) is atherosclerotic plaque rupture with resultant coronary thrombosis, posing a big burden in health care systems. Dual anti-platelet therapy (DAPT) can improve CV outcome with a prolonged regimen, albeit at the cost of increased bleeding rates. We performed a narrative literature review on the topic, in

which we explore databases through April 15th, 2020, with no restrictions on language. Key words of antiplatelet therapy, P2Y12 inhibitor, aspirin and DAPT were utilized. Randomized clinical trials, large prospective studies, systematic reviews and metanalysis were included. We hand-searched the reference lists of included articles and relevant reviews. The review revealed that when choosing antiplatelet agents, the decision should be driven by pharmacodynamic properties as well as demonstrated efficacy and safety. Additionally, it was noted that in patients undergoing percutaneous coronary intervention, prasugrel and ticagrelor are preferred. In patients with high risk of bleeds or receiving thrombolysis, or when cost or specific patient issues exist, clopidogrel is considered though is a second-line therapy. Due to an elevated risk of bleeds, triple therapy should be avoided, as evidence shows effectiveness and safety with regimens without ASA. Furthermore, multiple studies have also shown that regimens shorter than 12 months of DAPT could be adequate for many patients, and newer guidelines are likely going to reflect it. There are specific recommendations for switching among antiplatelets, mostly based on registries and pharmacodynamic studies.

[20] *Haluzík M, Hrádková V, Kudláčková M, Jakubíková I*. **Obesity treatment in patients both with and without diabetes: current options and perspectives**. Cas Lek Cesk 2020; 159:136-140.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33297689

ABSTRACT

Increasing prevalence of obesity and its complications in practically all developed countries worldwide is one of the most cardinal problems of current healthcare. Obesity is an important risk factor for the development of type 2 diabetes mellitus and it is closely interconnected with arterial hypertension, dyslipidemia and other diseases commonly referred to as metabolic syndrome or insulin resistance syndrome. Overall, this combination of diseases markedly increases risk of cardiovascular morbidity and mortality. In this paper, we provide a review of current possibilities of pharmacological modulation of body weight in patients with obesity both with and without diabetes. We also briefly mention the treatment possibilities using bariatric surgery and endoscopy, and discuss the perspectives of pharmacological modulation of body weight in patients with diabetes in the context of ongoing research programmes.

[21] *Gouda P, Welsh RC, Padarath M et al.* **Landscape of Lipid Management Following an Acute Coronary Syndrome Event: Survey of Canadian Specialists**. CJC Open 2020; 2:625-631.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33305223

ABSTRACT

BACKGROUND: Following the occurrence of an acute coronary syndrome (ACS), patients are at high risk for subsequent cardiovascular events. Therapies to lower the level of low-density lipoprotein (LDL) cholesterol remain a pillar in secondary prevention approaches following ACS. Significant variability remains in the application of therapies to lower cholesterol level in clinical practice. METHODS: A cross-sectional, online survey was conducted of 200 cardiovascular and lipid specialists across Canada who routinely care for patients following the occurrence of ACSs. The survey consisted of 50 multiple-choice questions with opportunities for free-text entry exploring knowledge of lipid guidelines and recent clinical trials, and in-hospital and outpatient management of lipids and familial hypercholesterolemia. RESULTS: A total of 67.5% (n = 135) of participants stated that a lipid panel would routinely be obtained during the first 24 hours of an admission for an ACS, and 68.5% (n = 137) stated that their hospitals had standing orders for statin initiation at ACS

presentation. In high-risk patients, the majority (75.5%; n = 151) of participants indicated that they target an LDL cholesterol level of <1.8 mmol/L. However, a subset (22%; n = 44) would target lower LDL cholesterol levels ranging from 0.5 to 1.7 mmol/L. Only 32.0% (n = 64) of participants stated that >70% of their ACS patients were at or below guideline-recommended LDL cholesterol levels. Respondents generally underappreciated the prevalence of familial hypercholesterolemia in both the general population and ACS patients. CONCLUSIONS: There is significant variation in practice patterns involving therapies to lower LDL cholesterol level in the post-ACS onset period. To improve management of lipids in this high-risk population, changes to institutional policies, shared responsibility of lipid management across multiple disciplines, and physician education are required.

[22] *Pace R, Harris S, Parry M, Zaran H*. **Primary and Secondary Cardiovascular Prevention Among First Nations Peoples With Type 2 Diabetes in Canada: Findings From the FORGE AHEAD Program**. CJC Open 2020; 2:547-554.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33305215
ABSTRACT
BACKGROUND: First Nations (FN) peoples in Canada face spiraling rates of type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD). Data on the extent of CVD risk-factor management in FN peoples with T2DM in Canada are scarce. METHODS: A T2DM registry with data from 7 FN communities in Canada was utilized to identify individuals eligible for primary and secondary CVD prevention. Proportions of individuals meeting clinical practice guideline-specified targets (hemoglobin A1c ≤7.0%; blood pressure ≤130/80 mm Hg; low-density lipoprotein ≤2 mmol/L) were calculated. Prescription of recommended cardioprotective medications (antithrombotic medication, lipid-lowering agents, renin-angiotensin-aldosterone system inhibitors, and beta-blockers) among those with CVD was assessed. $\chi(2)$ tests were employed to evaluate differences between CVD prevention groups and sexes. RESULTS: Of the 2098 individuals in the registry, 18% had documented CVD (female: male = 1.12). Overall, <10% met all 3 clinical practice guideline targets. Attainment of hemoglobin A1c and blood pressure targets was comparable between primary and secondary CVD prevention groups, with<50% achieving targets. A greater proportion of the secondary prevention group met low-density lipoprotein targets compared to those without CVD (61.6% vs 40.9%, $P < 0.01$). In the secondary prevention group, beta-blockers were prescribed to only 20%, and <60% were prescribed antithrombotics, lipid-lowering medications, or agents targeting the renin-angiotensin-aldosterone system; <2% were prescribed medications from all 4 classes of cardioprotective medications. CONCLUSIONS: Primary and secondary CVD prevention recommendations for individuals with T2DM are not being met for an alarmingly high proportion of FN peoples. These findings serve as an urgent call for proactive measures to reduce CVD events and related mortality in this high-risk population.

[23] *Alloubani A, Nimer R, Samara R*. **Relationship between Hyperlipidemia, Cardiovascular Disease and Stroke: a Systematic Review**. Current cardiology reviews 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33305711
ABSTRACT
BACKGROUND: Globally, dyslipidemia has been shown to be an independent predictor of many cardiovascular and cerebrovascular events, which lead to recent advocacy towards dyslipidemia prevention and control as a key risk factor and its prognostic significance to reduce the burden of

stroke and myocardial infarction. AIM: This study aimed to evaluate hyperlipidemia as a risk factor connected with stroke and CVD. Moreover, having identified this risk factor, the study evaluates how hyperlipidemia has been examined earlier and what can be done in the future. METHODS: All prospective studies concerning hyperlipidemia as risk factors for stroke and CVD were identified by a search of PubMed/MEDLINE and EMBASE databases with keywords hyperlipidemia, risk factors, stroke, and cardiovascular disease. RESULTS: The constant positive association between the incidence of coronary heart disease and cholesterol concentration of LDL is apparent in observational studies in different populations. Thus, the reduction of LDL cholesterol in those populations, particularly with regard to initial cholesterol concentrations, can reduce the risk of vascular diseases. However, the impact of using lipid-lowering drugs, such as statins, has been demonstrated in several studies as an important factor in decreasing the mortality and morbidity in rates of patients with stroke and CVD. CONCLUSION: After reviewing all the research mentioned in this review, it can be confirmed that hyperlipidemia is a risk factor for stroke and correlated in patients with CVD.

[24] *Mitsis A, Gragnano F*. **Myocardial Infarction with and without ST-segment Elevation: a Contemporary Reappraisal of Similarities and Differences**. Current cardiology reviews 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33305709

ABSTRACT

Understanding the similarities and differences between myocardial infarction with or without ST-segment elevation is an essential step for a proper patients' management in current practice. Both syndromes are caused by a critical stenosis or a total occlusion of coronary arteries (mostly due to thrombosis on atherosclerotic plaque), and manifest with a similar clinical presentation. Recent epidemiologic studies show that the relative incidence of ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation myocardial infarction (NSTEMI) moves in an opposite fashion (decreasing and increasing respectively), with a prognosis that is worse at short-term follow-up for STEMI but comparable at long-term. Current management differs, as for STEMIs an immediate reperfusion is recommended, while for NSTEMIs risk stratification is mandatory in order to stratify patients' risk, and then decide the timing for coronary angiography. Periprocedural and technical aspects of the interventional management as well antithrombotic medications are for the most similarly implemented in the two types of MI, with routine radial access, DES implant, and novel P2Y12 inhibitors representing the standard of care in both cases. The following review article aims to compare the two types of MI, with and without persistent ST-segment elevation. The main purpose is to explore their similarities and differences and address areas of uncertainty with regards to clinical presentation, therapeutic management, and prognosis. The identification of high-risk NSTEMI patients is important as they may require an individualised approach that can substantially overlap with current STEMI recommendations and their mortality remains high if their management is delayed.

[25] *Kos K*. **Cardiometabolic Morbidity and Mortality with Smoking Cessation, Review of Recommendations for People with Diabetes and Obesity**. Current diabetes reports 2020; 20:82.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33289870

ABSTRACT

PURPOSE OF REVIEW: Obesity is closely linked with the pathogenesis of type 2 diabetes (T2DM) and cardiovascular disease (CVD), and whilst smoking cessation is associated with weight gain, there

are concerns that this weight gain may offset the benefit of CVD risk reduction especially in those with considerable post-cessation weight gain. The aim of this narrative review is to evaluate recent evidence on smoking cessation and cardiometabolic outcomes and discuss limitations of current knowledge and studies. RECENT FINDINGS: Nicotine is a key player in modulating energy balance by influencing lipid storage in adipose tissue by affecting lipolysis, energy input by modulating appetite and energy output by increasing sympathetic drive and thermogenesis. It also increases insulin resistance and promotes abdominal obesity. The CVD risk and mortality associated with cigarette smoking potentiate the CVD risks in patients with diabetes. Evidence supports the benefit of quitting cigarette smoking regardless of any subsequent weight gain. Data suggests that the cardiometabolic risk is limited to the first few years and that cardiovascular health and mortality benefit of smoking cessation outweighs the harm related to weight gain. This weight gain can be limited by nicotine replacement of which e-cigarettes (vaping) are increasingly popular if it is not an alternative to cigarette smoking. However, long-term health data on e-cigarettes is needed prior to formal recommendation for its use in smoking cessation. The recommendation for cessation of cigarette smoking is justified for those at high risk of weight gain and diabetes. However, for most benefit, consideration should be given for personalized weight management to limit weight gain. Awareness of a 'lean paradox' by which lower weight is associated with increased CVD risk may help to improve motivation and insight into the bias of smoking, health and body composition otherwise known to epidemiologists as the 'obesity paradox'.

[26] *Constantinescu C, SĂndulescu L, SĂftoiu A*. **The Role of Elastography in Non-Alcoholic Fatty Liver Disease**. Current health sciences journal 2020; 46:255-269.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33304627
ABSTRACT
The most common liver disease in developing countries is non-alcoholic fatty liver disease (NAFLD). This involves the abnormal accumulation of lipids in the liver, the pathogenesis of the disease being related to dyslipidemia, obesity, insulin resistance and type 2 diabetes. Most often, the diagnosis of NAFLD is incidental, when performing routine blood tests or when performing a transabdominal ultrasound. The NAFLD spectrum ranges from simple forms of hepatic steatosis to the most advanced form of the disease, steatohepatitis (NASH), which in evolution can cause inflammation, fibrosis, cirrhosis of the liver and even liver cancer. For the evaluation of the prognosis and the clinical evolution, the most important parameter to define is the degree of liver fibrosis. Currently, the gold standard remains the liver biopsy, the differentiation between NAFLD and NASH being made only on the basis of histological analysis. However, liver biopsy is an invasive procedure, with numerous risks such as bleeding, lesions of the other organs and complications related to anesthesia, which significantly reduces its widespread use. Moreover, the risk of a false negative result and the increased costs of the procedure further limits its use in current practice. For this reason, non-invasive methods of evaluating the degree of liver fibrosis have gained ground in recent years. Imaging techniques such as elastography have shown promising results in evaluating and staging NAFLD. The aim of this article is to review the current status of the non-invasive tests for the assessment of NAFLD with a focus on the ultrasound-based elastography techniques.

[27] *Mäkinen S, Datta N, Nguyen YH et al.* **Simvastatin profoundly impairs energy metabolism in primary human muscle cells**. Endocrine connections 2020; 9:1103-1113.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33295884

ABSTRACT

OBJECTIVES: Simvastatin use is associated with muscular side effects, and increased risk for type 2 diabetes (T2D). In clinical use, simvastatin is administered in inactive lipophilic lactone-form, which is then converted to active acid-form in the body. Here, we have investigated if lactone- and acid-form simvastatin differentially affect glucose metabolism and mitochondrial respiration in primary human skeletal muscle cells. METHODS: Muscle cells were exposed separately to lactone- and acid-form simvastatin for 48 h. After pre-exposure, glucose uptake and glycogen synthesis were measured using radioactive tracers; insulin signalling was detected with Western blotting; and glycolysis, mitochondrial oxygen consumption and ATP production were measured with Seahorse XFe96 analyzer. RESULTS: Lactone-form simvastatin increased glucose uptake and glycogen synthesis, whereas acid-form simvastatin did not affect glucose uptake and decreased glycogen synthesis. Phosphorylation of insulin signalling targets Akt substrate 160 kDa (AS160) and glycogen synthase kinase 3β (GSK3β) was upregulated with lactone-, but not with acid-form simvastatin. Exposure to both forms of simvastatin led to a decrease in glycolysis and glycolytic capacity, as well as to a decrease in mitochondrial respiration and ATP production. CONCLUSIONS: These data suggest that lactone- and acid-forms of simvastatin exhibit differential effects on non-oxidative glucose metabolism as lactone-form increases and acid-form impairs glucose storage into glycogen, suggesting impaired insulin sensitivity in response to acid-form simvastatin. Both forms profoundly impair oxidative glucose metabolism and energy production in human skeletal muscle cells. These effects may contribute to muscular side effects and risk for T2D observed with simvastatin use.

[28] *Peer N, Baatiema L, Kengne AP*. **Ischaemic heart disease, stroke, and their cardiometabolic risk factors in Africa: current challenges and outlook for the future**. Expert review of cardiovascular therapy 2020:1-12.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33305637

ABSTRACT

INTRODUCTION: Although cardiovascular diseases (CVDs) are among the leading causes of death in Sub-Saharan Africa (SSA), prevention is not a priority and effective treatments are not widely available. This perspective discusses the burden, challenges, and potential opportunities for improvement of CVD prevention and control efforts in SSA. AREAS COVERED: This paper focuses on ischemic heart disease and stroke, and their key contributors of obesity, hypertension, diabetes and dyslipidaemia which are well-established, rapidly rising, and significant contributors to disease burden in SSA. However, their prevention, detection, treatment and control of are currently disorganized, inconsistent, unreliable, and insufficient with most SSA countries not geared to respond to this growing problem. National policies are frequently lacking or, if available, remain poorly implemented, for the control of these conditions. Primary healthcare systems have not adapted to cope with these rising CVD burdens and remain weak, underfunded and under resourced. Numerous barriers at the healthcare service, healthcare provider, and patient levels prevent optimal CVD risk factor care. EXPERT OPINION: Innovative approaches such as task-shifting with the reallocation of care to lower-level healthcare workers and the potential use of inexpensive technological options should be encouraged to provide equitable CVD preventive and curative solutions to SSA's poor.

[29] *Qin C, Minghan H, Ziwen Z, Yukun L*. **Alteration of lipid profile and value of lipids in the prediction of the length of hospital stay in COVID-19 pneumonia patients**. Food Sci Nutr 2020; 8:6144-6152.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33282265

ABSTRACT

To observe lipid profiles and their alterations in hospitalized patients with COVID-19 pneumonia (NCP) and evaluate the value of lipids for the prediction of the length of hospital stay (LOS), a total of 248 patients aged 18 years or older were enrolled in this retrospective study. At admission, the median levels of triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) in all patients were 1.11, 4.00, 0.89, and 2.11 mmol/L, respectively. Compared with common cases (n = 174), severe cases (n = 74) exhibited higher TG and HDL-C, and lower LDL-C. Levels of TC and LDL-C were negatively correlated with LOS. In 68 severe cases, serum lipids were followed up during hospitalization, and the median LOS was 29 days. The average levels of serum lipids were lowest at admission and gradually increased during hospitalization. Compared with the LOS ≤ 29 days group, serum levels of TC, HDL-C, and LDL-C were significantly lower in the LOS > 29 days group at admission; this lower trend was found in the subsequent tests for TC and LDL-C but not for HDL-C or TG. Multiple-variant COX regression showed that levels of TC or LDL-C at admission were independent risk of LOS prolongation. Together, these findings suggest that in patients with NCP, levels of TC and LDL-C at admission were negatively correlated with LOS. In severe cases, the gradual increase in TC, LDL-C, and HDL-C during hospitalization might indicate gradual recovery. TC < 3.75 mmol/L or LDL-C < 1.7 mmol/L at admission may act as an independent predictor of prolonged LOS.

[30] *Katzmann JL, Gouni-Berthold I, Laufs U*. **PCSK9 Inhibition: Insights From Clinical Trials and Future Prospects**. Front Physiol 2020; 11:595819.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33304274

ABSTRACT

In 2003, clinical observations led to the discovery of the involvement of proprotein convertase subtilisin/kexin type 9 (PCSK9) in lipid metabolism. Functional studies demonstrated that PCSK9 binds to the low-density lipoprotein (LDL) receptor directing it to its lysosomal degradation. Therefore, carriers of gain-of-function mutations in PCSK9 exhibit decreased expression of LDL receptors on the hepatocyte surface and have higher LDL cholesterol (LDL-C) levels. On the contrary, loss-of-function mutations in PCSK9 are associated with low LDL-C concentrations and significantly reduced lifetime risk of cardiovascular disease. These insights motivated the search for strategies to pharmacologically inhibit PCSK9. In an exemplary rapid development, fully human monoclonal antibodies against PCSK9 were developed and found to effectively reduce LDL-C. Administered subcutaneously every 2-4 weeks, the PCSK9 antibodies evolocumab and alirocumab reduce LDL-C by up to 60% in a broad range of populations either as monotherapy or in addition to statins. Two large cardiovascular outcome trials involving a total of ~46,000 cardiovascular high-risk patients on guideline-recommended lipid-lowering therapy showed that treatment with evolocumab and alirocumab led to a relative reduction of cardiovascular risk by 15% after 2.2 and 2.8 years of treatment, respectively. These findings expanded the armamentarium of pharmacological approaches to address residual cardiovascular risk associated with LDL-C. Furthermore, the unprecedented low LDL-C concentrations achieved (e.g., 30 mg/dL in the FOURIER study) suggest that the relationship

between LDL-C and cardiovascular risk is without a lower threshold, and without associated adverse events during the timeframe of the studies. The side effect profile of PCSK9 antibodies is favorable with few patients exhibiting injection-site reactions. Currently, the access to PCSK9 antibodies is limited by high treatment costs. The development of novel approaches to inhibit PCSK9 such as the use of small interfering RNA to inhibit PCSK9 synthesis seems promising and may soon become available.

[31] *Patwardhan VG, Mughal ZM, Padidela R et al.* **To study impact of treatment with Rosuvastatin versus Atorvastatin on 25 hydroxy Vitamin D concentrations among adult Indian men- a randomized control trial**. Indian journal of pharmacology 2020; 52:365-371.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33283767

ABSTRACT

BACKGROUND: Dyslipidemias are on the rise and are increasingly being treated with statins. As the metabolism of cholecalciferol and cholesterol are interrelated, reduction in cholesterol synthesis by statins is likely to affect Vitamin D status. OBJECTIVES: (1) The aim is to study the effect of treatment with statins (Atorvastatin/Rosuvastatin) on 25-hydroxy-Vitamin-D (25OHD) among newly detected subjects with dyslipidemia for 6 months (2) To study the impact of 25OHD concentrations on the efficacy of statin treatment. MATERIALS AND METHODS: This was a prospective, balanced randomized (1:1), open-label, parallel-group study, in apparently healthy Indian adult men (south Asian, 40-60 years). At baseline, serum lipids and 25OHD concentrations were measured. Based on the Adult Treatment Panel III guidelines, subjects were divided as per lipid concentrations into controls (who did not require statin treatment) and intervention (who required statin treatment) groups. Random allocation of subjects was done in two groups for receiving intervention for 6 months: Atorvastatin group (n = 52, received Atorvastatin) or Rosuvastatin group (n = 52, received Rosuvastatin). Lipids and 25OHD concentrations were measured at the end line. RESULTS: Atorvastatin group presented significant reduction ($P < 0.05$) in 25OHD, total cholesterol (TC) and low-density-lipoprotein-cholesterol (LDL-C) concentrations at the end line. In the Rosuvastatin group, significant drop in TC, LDL-C and high-density lipoprotein cholesterol (concentrations ($P < 0.05$) was observed, while 25OHD concentrations showed no significant change. Mean 25OHD concentrations were significantly correlated with a reduction in LDL-C concentrations in Atorvastatin group. CONCLUSIONS: Treatment with Atorvastatin resulted in a reduction in 25OHD concentrations; further, its efficacy in reducing LDL-C concentrations was related to the 25OHD concentrations.

[32] *Taberner-Cortés A, Vinué Á, Herrero-Cervera A et al.* **Dapagliflozin Does Not Modulate Atherosclerosis in Mice with Insulin Resistance**. International journal of molecular sciences 2020; 21.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33287201

ABSTRACT

Type 2 diabetes mellitus (T2DM) increases morbimortality in humans via enhanced susceptibility to cardiovascular disease (CVD). Sodium-glucose co-transporter 2 inhibitors (SGLT2i) are drugs designed for T2DM treatment to diminish hyperglycaemia by reducing up to 90% of renal tube glucose reabsorption. Clinical studies also suggest a beneficial action of SGLT2i in heart failure and CVD independent of its hypoglycaemiant effect. In the present study, we explored the effect of SGLT2i dapagliflozin (DAPA) in the metabolism and atherosclerosis in Apoe-/-Irs2+/- mice, which

display accelerated atherosclerosis induced by insulin resistance. DAPA treatment of Apoe-/-Irs2+/- mice, which were fed a high-fat, high-cholesterol diet, failed to modify body weight, plasma glucose or lipid. Carbohydrate metabolism characterisation showed no effect of DAPA in the glucose tolerance test (GTT) despite augmented insulin levels during the test. In fact, decreased C-peptide levels in DAPA-treated mice during the GTT suggested impaired insulin release. Consistent with this, DAPA treatment of Apoe-/-Irs2+/- isolated islets displayed lower glucose-stimulated insulin secretion compared with vehicle-treated islets. Moreover, insulin-signalling experiments showed decreased pAKT activation in DAPA-treated adipose tissue indicating impaired insulin signalling in this tissue. No changes were seen in lesion size, vulnerability or content of macrophages, vascular smooth muscle cells, T cells or collagen. DAPA did not affect circulating inflammatory cells or cytokine levels. Hence, this study indicates that DAPA does not protect against atherosclerosis in insulin-resistant mice in hypercholesterolemic conditions.

[33] *Mortensen MB, Dzaye O, Steffensen FH et al.* **Impact of Plaque Burden Versus Stenosis on Ischemic Events in Patients With Coronary Atherosclerosis**. Journal of the American College of Cardiology 2020; 76:2803-2813.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33303068
ABSTRACT
BACKGROUND: Patients with obstructive coronary artery disease (CAD) are at high risk for cardiovascular disease (CVD) events. However, it remains unclear whether the high risk is due to high atherosclerotic disease burden or if presence of stenosis has independent predictive value. OBJECTIVES: The purpose of this study was to evaluate if obstructive CAD provides predictive value beyond its association with total calcified atherosclerotic plaque burden as assessed by coronary artery calcium (CAC). METHODS: Among 23,759 symptomatic patients from the Western Denmark Heart Registry who underwent diagnostic computed tomography angiography (CTA), we assessed the risk of major CVD (myocardial infarction, stroke, and all-cause death) stratified by CAC burden and number of vessels with obstructive disease. RESULTS: During a median follow-up of 4.3 years, 1,054 patients experienced a first major CVD event. The event rate increased stepwise with both higher CAC scores and number of vessels with obstructive disease (by CAC scores: 6.2 per 1,000 person-years (PY) for CAC = 0 to 42.3 per 1,000 PY for CAC >1,000; by number of vessels with obstructive disease: 6.1 per 1,000 PY for no CAD to 34.7 per 1,000 PY for 3-vessel disease). When stratified by 5 groups of CAC scores (0, 1 to 99, 100 to 399, 400 to 1,000, and >1,000), the presence of obstructive CAD was not associated with higher risk than presence of nonobstructive CAD. CONCLUSIONS: Plaque burden, not stenosis per se, is the main predictor of risk for CVD events and death. Thus, patients with a comparable calcified atherosclerosis burden generally carry a similar risk for CVD events regardless of whether they have nonobstructive or obstructive CAD.

[34] *Claessen BE, Guedeney P, Gibson CM et al.* **Lipid Management in Patients Presenting With Acute Coronary Syndromes: A Review**. Journal of the American Heart Association 2020; 9:e018897.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33289416
ABSTRACT
Despite many improvements in its prevention and management, acute coronary syndrome (ACS) remains a major cause of morbidity and mortality in the developed world. Lipid management is an

important part of secondary prevention after ACS, but many patients currently remain undertreated and do not attain guideline-recommended levels of low-density lipoprotein cholesterol reduction. This review details the current state of evidence on lipid management in patients presenting with ACS, provides directions for identification of patients who may benefit from early escalation of lipid-lowering therapy, and discusses novel lipid-lowering medication that is currently under investigation in clinical trials. Moreover, a treatment algorithm aimed at attaining guideline-recommended low-density lipoprotein cholesterol levels is proposed. Despite important advances in the initial treatment and secondary prevention of ACS, ≈20% of ACS survivors experience a subsequent ischemic cardiovascular event within 24 months, and 5-year mortality ranges from 19% to 22%. Knowledge of the current state of evidence-based lipid management after ACS is of paramount importance to improve outcomes after ACS.

[35] *Friedman DJ*. **COVID-19 and APOL1: Understanding Disease Mechanisms through Clinical Observation**. Journal of the American Society of Nephrology : JASN 2021; 32:1-2.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33288631
ABSTRACT

[36] *Shaw LJ, Blankstein R, Bax JJ et al.* **Society of Cardiovascular Computed Tomography / North American Society of Cardiovascular Imaging - Expert Consensus Document on Coronary CT Imaging of Atherosclerotic Plaque**. Journal of cardiovascular computed tomography 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33303383
ABSTRACT
Coronary computed tomographic angiography (CCTA) provides a wealth of clinically meaningful information beyond anatomic stenosis alone, including the presence or absence of nonobstructive atherosclerosis and high-risk plaque features as precursors for incident coronary events. There is, however, no uniform agreement on how to identify and quantify these features or their use in evidence-based clinical decision-making. This statement from the Society of Cardiovascular Computed Tomography and North American Society of Cardiovascular Imaging addresses this gap and provides a comprehensive review of the available evidence on imaging of coronary atherosclerosis. In this statement, we provide standardized definitions for high-risk plaque (HRP) features and distill the evidence on the effectiveness of risk stratification into usable practice points. This statement outlines how this information should be communicated to referring physicians and patients by identifying critical elements to include in a structured CCTA report - the presence and severity of atherosclerotic plaque (descriptive statements, CAD-RADS™ categories), the segment involvement score, HRP features (e.g., low attenuation plaque, positive remodeling), and the coronary artery calcium score (when performed). Rigorous documentation of atherosclerosis on CCTA provides a vital opportunity to make recommendations for preventive care and to initiate and guide an effective care strategy for at-risk patients.

[37] *Farmakis I, Doundoulakis I, Pagiantza A et al.* **Lipoprotein(a) reduction with proprotein convertase subtilisin/kexin type 9 inhibitors: a systematic review and meta-analysis**. Journal of cardiovascular pharmacology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33298738

ABSTRACT
Lipoprotein(a) (Lp(a)) is a cardiovascular factor, for which there is no approved specific lowering treatment. Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors have been shown to have lowering effects on Lp(a). Aim of this systematic review is to synthesize the current literature and quantify the effects of PCSK9 inhibitors on the serum Lp(a) levels in human subjects.Double-blind, phase 2 or 3, randomized controlled trials comparing PCSK9 inhibitors (alirocumab or evolocumab) to placebo and/or ezetimibe and/or other lipid lowering therapy were deemed eligible for inclusion. We searched MEDLINE (via PubMed), CENTRAL, Scopus and Web of Science as of 17 June 2020. Quality assessment was performed using the Revised Cochrane risk-of-bias tool for randomized trials (RoB2).Forty-three studies were identified (64107 patients randomized) and 41 studies were included in the quantitative analysis. PCSK9 inhibitors reduced Lp(a) levels by -26.7% (95% CI -29.5% to -23.9%) with a significant heterogeneity within studies. There was significant difference in Lp(a) change from baseline according to comparator (placebo: mean -27.9%, 95% CI -31.1% to -24.6% vs. ezetimibe: mean -22.2%, 95% CI -27.2% to -17.2%, p=0.04) and duration of treatment (≤12 weeks: mean -30.9%, 95% CI -34.7% to -27.1% vs. >12 weeks: mean -21.9%, 95% CI -25.2% to -18.6%, p<0.01). Meta-regression analysis showed that only the mean percentage change from baseline LDL-C due to the intervention is significantly associated with the effect size difference (p<0.0001). PCSK9 inhibitors reduced LDL-C by -54% (95% CI -57.6% to -50.6%).There is substantial efficacy of the currently approved PCSK9 inhibitors in the lowering of Lp(a) levels. Dedicated RCTs are needed to establish the benefit of this intervention.

[38] *Zhou X, Wu L, Chen Y et al.* **48-week of statin therapy for T2DM patients with LEAD: comparison of the effects of pitavastatin and atorvastatin on lower femoral total plaque areas**. Journal of diabetes investigation 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33289308

ABSTRACT
AIMS: Type 2 diabetes mellitus (T2DM) is correlated with systemic atherosclerosis. Statin therapies have been proved to reduce low-density lipoprotein cholesterol (LDL-C) level, protecting T2DM patients from cardiovascular events. Recently, more interest has been focused on the regression of lower extremity atherosclerotic disease (LEAD) for the potential prevention of amputation. However, the effects of pitavastatin and atorvastatin on LEAD in T2DM patients have not been directly compared. METHODS: This study compared the effects of pitavastatin and atorvastatin on femoral total plaque areas (FTPA), and lipids and glucose metabolism in T2DM patients with elevated LDL-C level and LEAD. T2DM patients with LDL-C level > 2.6mmol/L and LEAD were randomly assigned to receive either pitavastatin 2mg/d or atorvastatin 10mg/d for 48 weeks. FTPA were measured at baseline and the end of the study. Levels of glucose and lipids profile were measured periodically. The efficacy was evaluated in 63 patients. RESULTS: The percent change in FTPA measurements were similar between pitavastatin group and atorvastatin group (-17.79±21.27% vs -14.34±16.33%), as were the changes in LDL-C (-44.0±18.0% vs -40.3±18.2%) and triglyceride (17.6±20.0% vs 16.2±17.0%). But the level of high-density lipoprotein cholesterol (HDL-C) was significantly higher in the pitavastatin group compared with the atorvastatin group after 48 weeks of treatment (12.9±10.3% vs 7.2±11.7%, P<0.05). There were no significant differences between groups for the measurements of glucose metabolism. CONCLUSION: In T2DM patients with elevated LDL-C level and LEAD, 48 weeks of treatment with either pitavastatin or atorvastatin was associated with significant regression

of FTPA. Pitavastatin treatment resulted in a significantly higher HDL-C level compared with atorvastatin treatment.

[39] *Dusuel A, Deckert V, Pais DEBJP et al.* **Human CETP lacks lipopolysaccharide transfer activity, but worsens inflammation and sepsis outcomes in mice**. Journal of lipid research 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33298531

ABSTRACT

Bacterial lipopolysaccharides (LPSs or endotoxins) can bind most proteins of the lipid transfer/LPS-binding protein (LT/LBP) family in host organisms. The LPS-bound LT/LBP proteins then trigger either an LPS-induced proinflammatory cascade or LPS binding to lipoproteins that are involved in endotoxin inactivation and detoxification. Cholesteryl ester transfer protein (CETP) is an LT/LBP member, but its impact on LPS metabolism and sepsis outcome is unclear. Here, we performed fluorescent LPS transfer assays to assess the ability of CETP to bind and transfer LPS. The effects of intravenous (iv) infusion of purified LPS or polymicrobial infection (cecal ligation and puncture [CLP]) were compared in transgenic mice expressing human CETP and wild-type mice naturally having no CETP activity. CETP displayed no LPS transfer activity in vitro, but it tended to reduce biliary excretion of LPS in vivo. The CETP expression in mice was associated with significantly lower basal plasma lipid levels and with higher mortality rates in both models of endotoxemia and sepsis. Furthermore, CETPTg plasma modified cytokine production of macrophages in vitro. In conclusion, despite having no direct LPS binding and transfer property, human CETP worsens sepsis outcomes in mice by altering the protective effects of plasma lipoproteins against endotoxemia, inflammation, and infection.

[40] *Dekkers IA, Bizino MB, Paiman EHM et al.* **The Effect of Glycemic Control on Renal Triglyceride Content Assessed by Proton Spectroscopy in Patients With Type 2 Diabetes Mellitus: A Single-Center Parallel-Group Trial**. J Ren Nutr 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33293204

ABSTRACT

OBJECTIVE: Ectopic lipid accumulation in the kidney (fatty kidney) is a potential driver of diabetic kidney disease, and tight glycemic control can reduce risk of diabetic nephropathy. We assessed whether glycemic control influences renal triglyceride content (RTGC). Furthermore, we compared glucagon-like peptide-1 receptor agonist liraglutide versus standard glucose-lowering therapy. DESIGN AND METHODS: In this single-center parallel-group trial, patients with type 2 diabetes mellitus were randomized to liraglutide or placebo added to standard care (metformin/sulfonylurea derivative/insulin). Changes in RTGC after 26 weeks of glycemic control measured by proton spectroscopy and difference in RTGC between treatment groups were analyzed. RESULTS: Fifty patients with type 2 diabetes mellitus were included in the baseline analysis (mean age, 56.5 ± 9.1 years; range, 33-73 years; 46% males). Seventeen patients had baseline and follow-up measurements. Mean glycated hemoglobin was 7.8 ± 0.8%, which changed to 7.3 ± 0.9% after 26 weeks of glycemic control irrespective of treatment group (P = .046). Log-transformed RTGC was -0.68 ± 0.30% and changed to -0.83 ± 0.32% after 26 weeks of glycemic control irrespective of treatment group (P = .049). A 26-week-to-baseline RTGC ratio (95% confidence interval) was significantly different between liraglutide (-0.30 [-0.50, -0.09]) and placebo added to standard care (-0.003 [-0.34, 0.34]) (P = .04). CONCLUSION: In this exploratory study, we found that 26 weeks of

glycemic control resulted in lower RTGC, in particular for liraglutide; however, larger clinical studies are needed to assess whether these changes reflect a true effect of glycemic control on fatty kidney.

[41] *Chen YM, Chen PK, Chang CK et al.* **Association of Apolipoprotein E Polymorphism with Adipokines and Cardiovascular Disease Risk in Rheumatoid Arthritis Patients**. Life (Basel) 2020; 10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33297350
ABSTRACT
Apolipoprotein E (ApoE) polymorphism and adipokines are linked to atherosclerosis. We aimed to investigate the associations of apoE genotypes with adipokines, inflammatory parameters, and cardiovascular disease (CVD) risks in rheumatoid arthritis (RA) patients. We enrolled 152 RA patients and 49 healthy control (HC) subjects. The apoE genotyping was determined by a polymerase chain reaction, while plasma levels of adipokines and inflammatory cytokines were measured with ELISA. Although apoE genotypes distributions were indistinguishable between RA patients and HC, we found significantly higher levels of apoE and adipokines in RA patients compared with HC. RA patients with ε2ε3 genotype had lower levels of TNF-α, IL-6, resistin, and visfatin, but higher leptin levels compared with ε3ε3 genotype patients. Patients with ε3ε4 genotype had significantly higher low-density lipoprotein-cholesterol (LDL-C) levels and atherogenic index scores compared with ε2ε3 genotype carriers. Moreover, patients with ε2ε3 genotype had significantly lower 10-year CVD risk than ε3ε3 or ε3ε4 genotype patients. ε3ε4 genotype and adiponectin levels were independent predictors of a high 10-year CVD risk. RA patients with ε2ε3 genotype are associated with lower levels of TNF-α, IL-6, resistin, visfatin, and CVD risk, while RA patients with ε3ε4 genotype exhibited higher levels of LDL-C, insulin resistance, and higher CVD risks.

[42] *Valanti EK, Dalakoura-Karagkouni K, Siasos G et al.* **Advances in biological therapies for dyslipidemias and atherosclerosis**. Metabolism 2020; 116:154461.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33290761
ABSTRACT
Atherosclerosis is a multifactorial disease influenced by genetics, lifestyle and environmental factors. Despite therapeutic advances that reduce the risk of cardiovascular events, atherosclerosis-related diseases remain the leading cause of mortality worldwide. Precise targeting of genes involved in lipoprotein metabolism is an emerging approach for atherosclerosis prevention and treatment. This article focuses on the latest developments, clinical potential and current challenges of monoclonal antibodies, vaccines and genome/transcriptome modification strategies, including antisense oligonucleotides, genome/base editing and gene therapy. Multiple lipid lowering biological therapies have already been approved by the FDA with impressive results to date, while many more promising targets are being pursued in clinical trials or pre-clinical animal models.

[43] *Martin SS*. **Factoring in ANGPTL3 When LDL Is Refractory**. The New England journal of medicine 2020; 383:2385-2386.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33296565
ABSTRACT

[44] *Cuadrado-Soto E, López-Sobaler AM, Jiménez-Ortega AI et al.* **Breakfast Habits of a Representative Sample of the Spanish Child and Adolescent Population (The ENALIA Study): Association with Diet Quality**. Nutrients 2020; 12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33302560
ABSTRACT
The association between breakfast quality and total diet quality of children and adolescents ((1-17.9 years (n = 1570)) from the National Dietary Survey on the Child and Adolescent Population in Spain (ENALIA) was analyzed. Dietary information was collected using two non-consecutive one-day food diaries (1-10 years old) or two 24 h dietary recalls (>10 years). Breakfast quality index (BQI) and a variant of Nutrient Rich Foods index (NRF9.3) were calculated to assess the total diet quality. Children and adolescents who had breakfast on at least one day (n = 1561) were divided into two groups according to BQI: Worse Quality Breakfast (WQB) (BQI < 4 points (P66), n = 781) and Good Quality Breakfast (GQB) (BQI ≥ 4, n = 780). Younger children and those whose parents have university education presented higher BQI. GQB group had significantly higher intakes of micronutrients (vitamins A, D, C, B(1), B(2), B(6), niacin, folate, calcium, potassium, magnesium). Fewer GQB children exceeded the Acceptable Macronutrient Distribution Range for fat and had folate and calcium intakes below their estimated average requirement. Daily NRF9.3 was 496.2 ± 54.0, being higher in GQB (503.8 ± 50.6 vs. 488.6 ± 56.2, p < 0.001). Increasing the quality of breakfast increased the possibility of having a NRF9.3 higher than P(50) (OR: 1.893, CI: 1.549-2.315, p < 0.0001). Breakfasts have room for quality improvement in a high percentage of children. A higher quality breakfast is associated with a benefit in the quality of the total diet.

[45] *Ayoub BM, Ashoush N, Tadros MM et al.* **Rosuvastatin dose should be case individualized: An observation from inherited hypercholesterolemia case study**. Pharmazie 2020; 75:531-532.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33305732
ABSTRACT

[46] *Fini NA, Bernhardt J, Churilov L et al.* **A 2-Year Longitudinal Study of Physical Activity and Cardiovascular Risk in Survivors of Stroke**. Phys Ther 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33305804
ABSTRACT
OBJECTIVE: The purpose of this study was to explore associations between physical activity, cardiovascular risk factors, mobility, mood, fatigue and cognition over 2 years following stroke rehabilitation discharge. METHODS: In this longitudinal observational study, survivors of first-ever stroke were evaluated at rehabilitation discharge, 6, 12, and 24 months later. Moderate to vigorous physical activity (MVPA) duration (minutes/day) assessed with an electronic monitor was the primary outcome. Further outcomes included step count, the number and duration of MVPA and sedentary bouts, cardiovascular risk factors (eg, blood pressure, fasting lipid profile, body mass index), gait speed and endurance, mood, fatigue, and cognition. Associations between physical activity and cardiovascular risk factors over time were assessed with random-effects regression modeling. Associations between baseline characteristics and physical activity at 2 years were explored using regression modeling. RESULTS: Seventy-nine participants (68.4% men) with a mean age of 65 years (SD = 14) and a median gait speed of 1.2 m/s (interquartile range = 0.8-1.4) were included at baseline. Associations were found between higher physical activity (MVPA duration, number and

duration of MVPA bouts) and lower body mass index. Better gait speed, endurance, and cognition at baseline were associated with higher MVPA and step count at 2 years. CONCLUSIONS: Duration and bouts of MVPA are associated with body mass index. Increasing MVPA and bouts of MVPA may be a valuable treatment goal to reduce cardiovascular risk in survivors of stroke. IMPACT: This 2-year study found that moderate to vigorous physical activity is associated with important cardiovascular risk factors in people who have survived stroke. Understanding these associations could be useful for developing effective treatments to prevent recurrent stroke.

[47] *Li H, Zhang X, Sun Q et al.* **Association between serum lipid concentrations and attempted suicide in patients with major depressive disorder: A meta-analysis**. PloS one 2020; 15:e0243847.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33301469
ABSTRACT
BACKGROUND: There is growing evidence that serum lipid concentrations may be associated with attempted suicide in patients with major depressive disorder (MDD), but these findings remain controversial. Thus, we performed a comprehensive meta-analysis to quantitatively assess the associations between serum lipid concentrations and attempted suicide in MDD patients. MATERIALS AND METHODS: Electronic databases (PubMed, Embase, the Cochrane Library and the China National Knowledge Library) were searched for relevant literature up to 10 February 2020. We used a random-effects model based on heterogeneity amongst studies and generated pooled standardised mean differences (SMDs). RESULTS: Thirty-two studies comprising 7,068 subjects met the inclusion criteria. A pooled analysis showed that compared with non-attempters, MDD patients who had attempted suicide had significantly lower serum concentrations of total cholesterol (TC) (SMD: -0.63, 95% CI: -0.83 to -0.44) and low-density lipoprotein cholesterol (LDL-C) (SMD: -0.69, 95% CI: -1.04 to -0.34), but the serum concentrations of high-density lipoprotein cholesterol (HDL-C) (SMD: -0.12, 95% CI: -0.33 to 0.10) and triglycerides (TGs) (SMD: 0.00, 95% CI: -0.20 to 0.20) were not significantly different between the two groups. Subgroup and meta-regression analysis indicated that heterogeneity with respect to TC concentrations may be due to different ages ($p = 0.041$) and sample sizes ($p = 0.016$) of studies, and that heterogeneity with respect to HDL-C concentrations may be partly due to different settings of studies ($p = 0.017$). CONCLUSIONS: This meta-analysis demonstrated that lower concentrations of TC and LDL-C, but not of HDL-C and TGs, were associated with attempted suicide in MDD patients. This indicates that TC and LDL-C may be useful as biological markers for predicting whether MDD patients may attempt to commit suicide.

[48] *de Armas-Rillo L, Quevedo-Abeledo JC, de Vera-González A et al.* **Proprotein convertase subtilisin/kexin type 9 in the dyslipidaemia of patients with axial spondyloarthritis is related to disease activity**. Rheumatology (Oxford, England) 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33295631
ABSTRACT
OBJECTIVE: Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a serine protease that regulates cholesterol metabolism and has been linked to cardiovascular (CV) risk. The purpose of the present study was to examine whether PCSK9 levels are related to abnormalities in the lipid profile and the development of atherosclerosis that occurs in patients with axial SpA (axSpA). METHODS: We performed a cross-sectional study that encompassed 545 individuals; 299 patients with axSpA

and 246 statin use-matched controls. PCSK9 and standard lipid profiles were analysed in patients and controls. Carotid intima-media thickness (cIMT) and carotid plaques were assessed in patients. A multivariable analysis, adjusted for standard CV risk factors, was performed to evaluate the influence of PCSK9 on axSpA-related dyslipidaemia and subclinical carotid atherosclerosis. RESULTS: Total cholesterol, high-density lipoprotein and low density lipoprotein cholesterol, lipoprotein (a) and apolipoprotein A1 were significantly lower in axSpA patients than controls. PCSK9 serum levels [β coefficient -44 ng/dl (95% CI -60, -27), P = 0.000] were also downregulated in axSpA patients after fully multivariable adjustment. ASDAS-CRP was found to be independently and significantly related to PCSK9 [β coefficient 10 ng/dl (95% CI 1, 18), P = 0.023] after analysing fully adjusted models that took age, sex and the rest of the lipid profile molecules into account. Whereas patients taking prednisone showed higher serum levels of PCSK9 [55 ng/ml (95% CI 24, 8), P = 0.001], those under anti-TNF-α therapies exhibited lower levels [β coefficient -26 ng/ml (95% CI -43, -9], P = 0.003]. CONCLUSION: PCSK9 is downregulated in patients with axSpA. Disease activity is positive and significantly related to PSCK9. Anti-TNF-therapy yields a reduction in PCSK9 serum levels.

[49] *Farag HAM, Baqi HR, Qadir SA et al.* **Effects of Ramadan fasting on anthropometric measures, blood pressure, and lipid profile among hypertensive patients in the Kurdistan region of Iraq**. SAGE open medicine 2020; 8:2050312120965780.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33294186
ABSTRACT
OBJECTIVE: This study was employed to assess the effects of Ramadan fasting on anthropometric measures, blood pressure, and lipid profile among hypertensive patients. METHOD: This cross-sectional study was conducted among a representative sample, which was selected using a census survey of hypertensive patients (both gender, aged 25-50 years, on regular antihypertensive drugs (atenolol: 50 mg orally once a day)), during Ramadan month that was falling in April to May 2020. The patients were receiving care at Halabja hospital in the Kurdistan region of Iraq. All patients were assessed in two phase's baseline (a week before Ramadan) and end stage (a week after Ramadan), using anthropometric indices, physical examination, biochemical tests, and a structured questionnaire. Statistical analysis was performed using SPSS version 21. RESULTS: A total of 120 hypertensive patients were included in the study (50% females and 50% males), with a mean age of 37.5 ± 6.6 years. The major finding of our study was the significant decrease in blood pressure (P < 0.001). Furthermore, the body weight, body mass index, and waist circumference of the participants decreased after Ramadan fasting in a significant approach (P < 0.001 for all). However, for the lipid profile components, the total cholesterol, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol change persisted not statistically significant (P > 0.05), while only triglyceride decreased drastically after Ramadan fasting (P < 0.001). CONCLUSION: Ramadan fasting could contribute in the improvement of blood pressure and lowers triglyceride levels, body weight, body mass index, and waist circumference of adult hypertensive patients.

[50] *Li W.* **Association of APOE E2 and low-density lipoprotein with depressive symptoms in Chinese senile schizophrenia inpatients: A cross-sectional study**. Schizophr Res Cogn 2021; 23:100193.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33294393
ABSTRACT

BACKGROUND: Schizophrenia is considered to occur due to both environmental and genetic factors. Depressive symptoms and apolipoprotein E (APOE) gene polymorphisms are involved in the pathogenesis of schizophrenia. However, the effect of APOE gene polymorphism on depressive symptoms has never been investigated among Chinese elderly schizophrenia patients. OBJECTIVE: This cross-sectional study aimed to determine the effect of APOE gene polymorphism on blood lipid metabolism and depressive symptoms among elderly schizophrenia patients. METHOD: A total of 301 elderly schizophrenia patients (161 males, age ranges from 60 to 92 years, with an average age of 67.31 ± 6.667) were included in the study. Depressive symptoms were assessed using the Geriatric Depression Scale (GDS). APOE gene polymorphisms were determined by polymerase chain reaction (PCR). Correlations between GDS and serum low-density lipoprotein (LDL) levels with APOE genotypes were assessed. RESULTS: The concentration of LDL in the APOE E2 group was significantly lower than those in the APOE E3 and APOE E4 groups, and the GDS scores in the APOE E2 and APOE E3 groups were higher than those in the APOE E4 group. Using partial correlation analysis and controlling the duration of disease and hyperlipidemia, we found that GDS scores were significantly correlated with LDL ($r = -0.179$, $p = 0.025$). CONCLUSIONS: The APOE E2 genotype is associated with more depressive symptoms and lower serum LDL in elderly Chinese schizophrenia patients, and there is a negative correlation between depressive symptoms and LDL.

[51] *Jurtz VI, Skovbjerg G, Salinas CG et al.* **Deep learning reveals 3D atherosclerotic plaque distribution and composition**. Scientific reports 2020; 10:21523.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33299076
ABSTRACT
Complications of atherosclerosis are the leading cause of morbidity and mortality worldwide. Various genetically modified mouse models are used to investigate disease trajectory with classical histology, currently the preferred methodology to elucidate plaque composition. Here, we show the strength of light-sheet fluorescence microscopy combined with deep learning image analysis for characterising and quantifying plaque burden and composition in whole aorta specimens. 3D imaging is a non-destructive method that requires minimal ex vivo handling and can be up-scaled to large sample sizes. Combined with deep learning, atherosclerotic plaque in mice can be identified without any ex vivo staining due to the autofluorescent nature of the tissue. The aorta and its branches can subsequently be segmented to determine how anatomical position affects plaque composition and progression. Here, we find the highest plaque accumulation in the aortic arch and brachiocephalic artery. Simultaneously, aortas can be stained for markers of interest (for example the pan immune cell marker CD45) and quantified. In ApoE-/- mice we observe that levels of CD45 reach a plateau after which increases in plaque volume no longer correlate to immune cell infiltration. All underlying code is made publicly available to ease adaption of the method.

[52] *Urbano F, Bugliani M, Filippello A et al.* **Author Correction: Atorvastatin but Not Pravastatin Impairs Mitochondrial Function in Human Pancreatic Islets and Rat β-Cells. Direct Effect of Oxidative Stress**. Scientific reports 2020; 10:22034.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33303887
ABSTRACT

[53] *Sánchez-Pérez H, Quevedo-Abeledo JC, Tejera-Segura B et al.* **Proprotein convertase subtilisin/kexin type 9 is related to disease activity and damage in patients with systemic erythematosus lupus**. Ther Adv Musculoskelet Dis 2020; 12:1759720x20975904.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33294038

ABSTRACT

BACKGROUND: Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a serine protease that regulates cholesterol metabolism through low-density lipoprotein receptor degradation and that has been linked to cardiovascular (CV) disease. The purpose of the present study was to examine whether PCSK9 levels are disrupted compared with controls in patients with systemic lupus erythematosus (SLE). We additionally sought to establish whether PCSK9 is related to both the abnormalities in the lipid profile and to the disease activity or damage of patients with SLE. METHODS: We performed a cross-sectional study that encompassed 366 individuals: 195 SLE patients and 171 age-, sex-, and statin intake-matched controls. PCSK9, lipoproteins serum concentrations, and lipid profiles were assessed in patients and controls. A multivariable analysis, adjusted for standard CV risk factors, was performed to evaluate the role of PCSK9 in SLE-related dyslipidemia. RESULTS: Most lipid related-molecules were decreased in patients with SLE compared with controls. This downregulation included PCSK9, with PCSK9 levels being lower in patients than controls in the full multivariable analysis, including the modifications in lipid profiles that the disease itself produces {beta coefficient -73 [95% confidence interval (CI) -91 to -54] ng/ml, $p \leqslant 0.001$}. Both SLICC and SLEDAI scores were independently and positively related to PCSK9. Patients currently on hydroxychloroquine exhibited decreased levels of PCSK9 compared with those that were not taking hydroxychloroquine [beta coefficient -30 (95% CI -54 to -6) ng/ml, $p = 0.015$]. CONCLUSION: PCSK9 is downregulated in SLE compared with controls, but SLE patients with higher disease activity and damage exhibited higher PSCK9 serum levels.

[54] *He L, Du X, Wang WH, Ma CS*. **[Comparison of compliance and cost effectiveness between brand-name statins and generic statins]**. Zhonghua liu xing bing xue za zhi = Zhonghua liuxingbingxue zazhi 2020; 41:1900-1904.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33297658

ABSTRACT

Objective: To explore the differences of adherence, lipid reduction and cost-effectiveness between brand-name and generic statins. Methods: Statins prescription records of adult patients aged 18 years and above with the first prescription of statins between January 2015 to December 2017, were collected from community health information system of Chaoyang district of Beijing. Medication compliancy after first prescription was compared between group only taking brand-name statins (41 496 records) and group only taking generic statins (60 491 records). Lipid reduction and cost-effectiveness were also compared between two groups. Results: The medication compliancy of generic statins was worse than brand-name statins (28.2% vs. 36.2%, $P<0.001$). After excluding the influence of age, sex, history of hypertension and diabetes, and community correlation, generic atorvastatin (20 mg/day) showed better total cholesterol reduction effect [(0.86±0.07) mmol/L] and better low density lipid-cholesterol reduction effect [(0.67±0.07) mmol/L] one year later in 199 patients who consistently used it compared with brand-name atorvastatin at same dosage in 232 patients [(0.40±0.10) mmol/L and (0.42±0.08) mmol/L] ($P<0.001$, $P=0.003$). From the perspective of cost effectiveness, generic atorvastatin (20 mg/day) can reduce more than 50% of medical expenses at

the same cholesterol reduction level. Conclusions: Generic statins might replace brand-name statins with similar treatment effect but lower medical expenses although its compliancy needs improvement. However, the data of adverse reactions of generic statins are lacking, it is necessary to carry out high-quality clinical research to improve and promote the development of generic statins.