[1] *Kaul S, Gupta M, Bandyopadhyay D et al.* **Gout Pharmacotherapy in Cardiovascular Diseases: A Review of Utility and Outcomes**. American journal of cardiovascular drugs : drugs, devices, and other interventions 2020:1-14.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33369719
ABSTRACT
Hyperuricemia and gout have been linked to an increased risk for cardiovascular (CV) disease, stroke, hypertension, heart failure, and chronic kidney disease, possibly through a proinflammatory milieu. However, not all the drugs used in gout treatment improve CV outcomes; colchicine has shown improved CV outcomes in patients with recent myocardial infarction and stable coronary artery disease independent of lipid-lowering effects. There is resurging interest in colchicine following publication of the COLCOT, LoDoCo, LoDoCo2, LoDoCo-MI trials, and COLCORONA trial which will shed light on its utility in COVID-19. Our aim is to review the CV use of colchicine beyond pericardial diseases, as well as CV outcomes of the available gout therapies, including allopurinol and febuxostat. The CARES trial and its surrounding controversies, which lead to the US FDA 'black box' warning on febuxostat, in addition to the recent FAST trial which contradicts this and finds febuxostat to be non-inferior, are discussed in this paper.

[2] *Simons N, Veeraiah P, Simons P et al.* **Effects of fructose restriction on liver steatosis (FRUITLESS); a double-blind randomized controlled trial**. The American journal of clinical nutrition 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33381794
ABSTRACT
BACKGROUND: There is an ongoing debate on whether fructose plays a role in the development of nonalcoholic fatty liver disease. OBJECTIVES: The aim of this study was to investigate the effects of fructose restriction on intrahepatic lipid (IHL) content in a double-blind randomized controlled trial using an isocaloric comparator. METHODS: Between March 2017 and October 2019, 44 adult overweight individuals with a fatty liver index ≥ 60 consumed a 6-wk fructose-restricted diet (<7.5 g/meal and <10 g/d) and were randomly assigned to supplementation with sachets of glucose (= intervention group) or fructose (= control group) 3 times daily. Participants and assessors were blinded to the allocation. IHL content, assessed by proton magnetic resonance spectroscopy, was the primary outcome and glucose tolerance and serum lipids were the secondary outcomes. All measurements were conducted in Maastricht University Medical Center. RESULTS: Thirty-seven participants completed the study protocol. After 6 wk of fructose restriction, dietary fructose intake and urinary fructose excretion were significantly lower in the intervention group (difference: -57.0 g/d; 95% CI: -77.9, -39.5 g/d; and -38.8 μmol/d; 95% CI: -91.2, -10.7 μmol/d, respectively). Although IHL content decreased in both the intervention and control groups ($P < 0.001$ and $P = 0.003$, respectively), the change in IHL content was more pronounced in the intervention group (difference: -0.7% point, 95% CI: -2.0, -0.03% point). The changes in glucose tolerance and serum lipids were not significantly different between groups. CONCLUSIONS: Six weeks of fructose restriction per se led to a small, but statistically significant, decrease in IHL content in comparison with an isocaloric control group.This trial was registered at clinicaltrials.gov as NCT03067428.

[3] *Anastasiou G, Sakka E, Blathra E et al.* **Lipoprotein(a): A Concealed Precursor of Increased Cardiovascular Risk? A Real-World Regional Lipid Clinic Experience**. Arch Med Res 2020.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33380360

ABSTRACT

OBJECTIVE: Lipoprotein(a) [Lp(a)] is an independent cardiovascular risk factor. We present real-life characteristics of patients with increased Lp(a) levels attending a University Lipid Clinic. METHODS: We retrospectively studied patients attending the University of Ioannina Hospital Lipid Clinic with Lp(a) levels ≥30 mg/dL who were followed-up for a median of 22 months. RESULTS: One hundred eight patients (median age 59 years, 49% females) were included with median Lp(a) levels 67 mg/dL (30-320). Of patients, 25.1% had established atherosclerotic cardiovascular disease (ASCVD): 11.1 and 5.6% positive personal history of myocardial infarction (MI) and stroke, respectively, 6.5% carotid artery disease and 1.9% lower extremities arterial disease (LEAD). In addition, 35.2% of participants had heterozygous familial hypercholesterolemia (heFH), 37.9% positive family history of premature ASCVD, 29.6% hypertension, 12.0% diabetes and 5.5% chronic kidney disease (CKD). Of patients, 67.6% were receiving statin therapy and 16.6% additional ezetimibe at baseline visit, and 83 and 35% were receiving statin treatment and additional ezetimibe, respectively, during follow-up. Low-density cholesterol (LDL-C) levels and LDL-C(corrected for Lp(a)) levels were significantly reduced in lipid-lowering therapy naive patients by 37 and 40% ($p < 0.05$), in lipid-lowering therapy intensified patients by 31 and 36% ($p < 0.05$), and in patients on stable lipid-lowering treatment by 15% ($p < 0.05$) and 10% ($p > 0.05$), respectively, during follow-up. Lp(a) levels increased by 9% ($p < 0.05$). CONCLUSION: Our data confirm the high prevalence of established ASCVD, hFH and positive familial history of premature ASCVD in patients with elevated Lp(a) levels. Lp(a) levels slightly increased during follow-up.

[4] **Correction to: Novel PCSK9 (Proprotein Convertase Subtilisin Kexin Type 9) Variants in Patients With Familial Hypercholesterolemia From Cape Town**. Arteriosclerosis, thrombosis, and vascular biology 2021; 41:e77.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33356374

ABSTRACT

[5] *Taskinen MR, Björnson E, Kahri J et al.* **Effects of Evolocumab on the Postprandial Kinetics of Apo (Apolipoprotein) B100- and B48-Containing Lipoproteins in Subjects With Type 2 Diabetes**. Arteriosclerosis, thrombosis, and vascular biology 2020:Atvbaha120315446.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33356392

ABSTRACT

OBJECTIVE: Increased risk of atherosclerotic cardiovascular disease in subjects with type 2 diabetes is linked to elevated levels of triglyceride-rich lipoproteins and their remnants. The metabolic effects of PCSK9 (proprotein convertase subtilisin/kexin 9) inhibitors on this dyslipidemia were investigated using stable-isotope-labeled tracers. Approach and Results: Triglyceride transport and the metabolism of apos (apolipoproteins) B48, B100, C-III, and E after a fat-rich meal were investigated before and on evolocumab treatment in 13 subjects with type 2 diabetes. Kinetic parameters were determined for the following: apoB48 in chylomicrons; triglyceride in VLDL(1) (very low-density lipoprotein) and VLDL(2); and apoB100 in VLDL(1), VLDL(2), IDL (intermediate-density lipoprotein), and LDL (low-density lipoprotein). Evolocumab did not alter the kinetics of apoB48 in chylomicrons or apoB100 or triglyceride in VLDL(1). In contrast, the fractional catabolic rates of VLDL(2)-apoB100 and VLDL(2)-triglyceride were both increased by about 45%, which led to a 28% fall in the VLDL(2)

plasma level. LDL-apoB100 was markedly reduced by evolocumab, which was linked to metabolic heterogeneity in this fraction. Evolocumab increased clearance of the more rapidly metabolized LDL by 61% and decreased production of the more slowly cleared LDL by 75%. ApoC-III kinetics were not altered by evolocumab, but the apoE fractional catabolic rates increased by 45% and the apoE plasma level fell by 33%. The apoE fractional catabolic rates was associated with the decrease in VLDL(2)- and IDL-apoB100 concentrations. CONCLUSIONS: Evolocumab had only minor effects on lipoproteins that are involved in triglyceride transport (chylomicrons and VLDL(1)) but, in contrast, had a profound impact on lipoproteins that carry cholesterol (VLDL(2), IDL, LDL). Registration: URL: https://www.clinicaltrials.gov; Unique identifier: NCT02948777.

[6] *Majeed K, Bellinge JW, Butcher SC et al.* **Coronary (18)F-sodium fluoride PET detects high-risk plaque features on optical coherence tomography and CT-angiography in patients with acute coronary syndrome**. Atherosclerosis 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33358367
ABSTRACT
BACKGROUND AND AIMS: (18)F-Sodium Fluoride Positron Emission Tomography ((18)F-NaF PET) non-invasively detects micro-calcification activity, the earliest stage of atherosclerotic arterial calcification. We studied the association between coronary (18)F-NaF uptake and high-risk plaque features on intra-coronary optical coherence tomography (OCT) and CT-angiography (CTCA) and the potential application to patient-level risk stratification. METHODS: Sixty-two prospectively recruited patients with acute coronary syndrome (ACS) underwent multi-vessel OCT, (18)F-NaF PET and CTCA. The maximum tissue to background ratio (TBRmax = standardised uptake value (SUV)max/SUVbloodpool) was measured in each coronary segment on (18)F-NaF PET scans. High-risk plaque features on OCT and CTCA were compared in matched coronary segments. The number of patients testing positive (>2SD above the normal range) for micro-calcification activity was determined. RESULTS: In 62 patients (age, mean ± standard deviation (SD) = 61 ± 9 years, 85% male) the coronary segments with elevated (18)F-NaF uptake had higher lipid arc (LA) (median [25th-75th centile]: 74° [35°-117°] versus 48° [15°-83°], p=0.021), higher prevalence of macrophages [n(%): 37 (62%) versus 89 (39%), p=0.008] and lower plaque free wall (PFW) (50° [7°-110°] versus 94° [34°-180°], p=0.027) on OCT, and a higher total plaque burden (p=0.011) and higher dense calcified plaque burden (p= 0.001) on CTCA, when compared with (18)F-NaF negative segments. Patients grouped by increasing number of coronary lesions positive for microcalcification activity (0,1, ≥2) showed decreasing plaque free wall, increasing calcification and increasing macrophages on OCT (respectively p=0.008, p < 0.001 and p=0.028). CONCLUSIONS: (18)F-NaF uptake is associated with high-risk plaque features on OCT and CTCA in a per-segment and per-patient analysis in subjects hospitalized for ACS.

[7] *Testa G, Staurenghi E, Giannelli S et al.* **Up-regulation of PCSK6 by lipid oxidation products: A possible role in atherosclerosis**. Biochimie 2021; 181:191-203.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33359561
ABSTRACT
Atherosclerosis is a degenerative disease characterized by lesions that develop in the wall of large- and medium-sized arteries due to the accumulation of low-density lipoproteins (LDLs) in the intima. A growing bulk of evidence suggests that cholesterol oxidation products, known as oxysterols, and the

aldehyde 4-hydroxy-2-nonenal (HNE), the major pro-atherogenic components of oxidized LDLs, significantly contribute to atherosclerotic plaque progression and destabilization, with eventual plaque rupture. The involvement of certain members of the protein convertase subtilisin/kexin proteases (PCSKs) in atherosclerosis has been recently hypothesized. Among them, PCSK6 has been associated with plaque instability, mainly thanks to its ability to stimulate the activity of matrix metalloproteinases (MMPs) involved in extracellular matrix remodeling and to enhance inflammation. In U937 promonocytic cells and in human umbilical vein endothelial cells, an oxysterol mixture and HNE were able to up-regulate the level and activity of PCSK6, resulting in MMP-9 activation as demonstrated by PCSK6 silencing. Inflammation, enhanced by these lipid oxidation products, plays a key role in the up-regulation of PCSK6 activity as demonstrated by cell pretreatment with NS-398, with epigallocatechin gallate or with acetylsalicylic acid, all with anti-inflammatory effects. For the first time, we demonstrated that both oxysterols and HNE, which substantially accumulate in the atherosclerotic plaque, up-regulate the activity of PCSK6. Of note, we also suggest a potential association between PCSK6 activity and MMP-9 activation, pointing out that PCSK6 could contribute to atherosclerotic plaque development.

[8] *Hou M, Zhou W, Sun L et al.* **Effect of Fish Oil on Insulin Sensitivity in Children: A Systematic Review and Meta-Analysis of Randomized, Controlled Trials**. Canadian journal of diabetes 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33388274

ABSTRACT

OBJECTIVES: Fish oil has been shown to reduce the risk of metabolic disorders. However, the effects of fish oil intervention on glucose metabolism and insulin sensitivity are still controversial, especially in children. The current meta-analysis aimed to evaluate the effects of fish oil intervention on insulin sensitivity in children. METHODS: The Cochrane Library, PubMed, Embase, Web of Science, ClinicalTrials.gov and China National Knowledge Infrastructure databases were searched up to August 2020 for relevant studies evaluating fish oil intake compared with placebo on insulin sensitivity indications (Homeostatic Model for Insulin Resistance). A fixed-effects model was used to calculate the pooled effect. RESULTS: A total of 13 studies with 1,132 participants (567 in placebo group and 565 in fish oil group) were included in the meta-analysis. Compared with the placebo group, fish oil intervention had beneficial effects on insulin sensitivity in the pooled analysis (weighted mean difference, -0.219; 95% confidence interval, -0.392 to -0.046; p=0.013). In subgroup analyses, when the fish oil intervention period was short-term (≤6 months) low dose (eicosapentaenoic acid + docosahexaenoic acid dose <1.5 g/day) and high ratio (eicosapentaenoic acid to docosahexaenoic acid ≥1), it could improve insulin sensitivity. No heterogeneity was found for the pooled and subgroup analyses. CONCLUSION: Fish oil intervention has a beneficial effect on insulin sensitivity in children.

[9] *Maffei E, Punzo B, Cavaliere C et al.* **Coronary atherosclerosis as the main endpoint of non-invasive imaging in cardiology: a narrative review**. Cardiovascular diagnosis and therapy 2020; 10:1897-1905.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33381433

ABSTRACT

The change of paradigm determined by the introduction of cardiac computed tomography (CCT) in the field of cardiovascular medicine has allowed new evidence to emerge. These evidences point towards a major role, probably the most important one in terms of prognostic impact, in the detection,

characterization and quantification of atherosclerosis as the main driver and endpoint for the management of coronary artery disease (CAD). Extensive literature has been published in the last decade with large numbers and patients' populations, investigating several aspects and correlations between atherosclerotic plaque features and risk factors; also, the relationship between plaque features, both with qualitative and quantitative approaches, and cardiovascular events has been investigated. More recent studies have also pointed out the relationship between the knowledge and classification of sub-clinical atherosclerosis and the induced modification of medical therapy (both aggressiveness and compliance) that is most likely able to increase the effect of anti-atherosclerotic drugs, hence significantly improving prognosis. Non-invasive assessment of CAD by means of CCT is becoming the primary tool for management and also the most important parameter for the comprehension of natural history of CAD and how the therapies we adopt are affecting plaque burden as a whole. In this review we will address the modern concepts of CAD driven understanding and management of cardiovascular disease.

[10] *Seitun S, Clemente A, De Lorenzi C et al.* **Cardiac CT perfusion and FFR(CTA): pathophysiological features in ischemic heart disease**. Cardiovascular diagnosis and therapy 2020; 10:1954-1978.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33381437
ABSTRACT
Cardiac computed tomography (CCT) has rapidly evolved, becoming a powerful integrated tool for the evaluation of coronary artery disease (CAD), and being superior to other noninvasive methods due to its high accuracy and ability to simultaneously assess both lumen stenosis and atherosclerotic plaque burden. Furthermore, CCT is regarded as an effective gatekeeper for coronary angiography, and carries independent important prognostic information. In the last decade, the introduction of new functional CCT applications, namely CCT perfusion (CCTP) imaging and CT-derived fractional flow reserve (FFR(CTA)), has opened the door for accurate assessment of the haemodynamic significance of stenoses. These new CCT technologies, thus, share the unique advantage of assessing both myocardial ischemia and patient-specific coronary artery anatomy, providing an integrated anatomical/functional analysis. In the present review, starting from the pathophysiology of myocardial ischemia, we evaluate the existing evidence for functional CCT imaging and its value in relation to alternative, well-established, non-invasive imaging modalities and invasive indices of ischemia (currently the gold-standard). The knowledge of clinical applications, benefits, and limitations of these new CCT technologies will allow efficient and optimal use in clinical practice in the near future.

[11] **Correction to: PCSK9 (Proprotein Convertase Subtilisin/Kexin 9) Enhances Platelet Activation, Thrombosis, and Myocardial Infarct Expansion by Binding to Platelet CD36**. Circulation 2021; 143:e4.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33378240
ABSTRACT

[12] *Silverstein RL*. **PCSK9 (Proprotein Convertase Subtilisin/Kexin 9) Goes "DAMP"**. Circulation 2021; 143:62-64.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33378238

ABSTRACT

[13] *Groth NA, Stone NJ, Benziger CP*. **Cardiology clinic visit increases likelihood of evidence-based cholesterol prescribing in severe hypercholesterolemia**. Clinical cardiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33355940

ABSTRACT
BACKGROUND: Patients with phenotypic severe hypercholesterolemia (SH), low-density lipoprotein-cholesterol (LDL-c) ≥ 190 mg/dl, atherosclerotic cardiovascular disease (ASCVD) or adults 40-75 years with diabetes with risk factors or 10-year ASCVD risk ≥20% benefit from maximally tolerated statin therapy. Rural patients have decreased access to specialty care, potentially limiting appropriate treatment. HYPOTHESIS: Prior visit with cardiology will improve treatment of severe hypercholesterolemia. METHODS: We used an electronic medical record-based SH registry defined as ever having an LDL-c ≥ 190 mg/dl since January 1, 2000 (n = 18 072). We excluded 3205 (17.7%) patients not alive or age 20-75 years. Patients defined as not seen by cardiology if they had no visit within the past 3 years (2017-2019). RESULTS: We included 14 867 patients (82.3%; mean age 59.7 ± 10.3 years; 58.7% female). Most patients were not seen by cardiology (n = 13 072; 72.3%). After adjusting for age, sex, CVD, hypertension, diabetes and obesity, patients seen by cardiology were more likely to have any lipid-lowering medication (OR = 1.46, 95% CI: 1.29-1.65), high-intensity statin (OR = 1.81, 95% CI: 1.61-2.03), or proprotein convertase subtilisin-kexin type 9 (PCSK9) inhibitor (OR = 5.96, 95% CI: 3.34-10.65) compared to those not seen by cardiology. Mean recent LDL-c was lower in patients seen by cardiology (126.8 ± 51.6 mg/dl vs. 152.4 ± 50.2 mg/dl, respectively; p < .001). CONCLUSION: In our predominantly rural population, a visit with cardiology improved the likelihood to be prescribed any statin, a high-intensity statin, or PCSK9 inhibitor. This more appropriately addressed their high life-time risk of ASCVD. Access to specialty care could improve SH patient's outcomes.

[14] *Su X, Cheng Y, Chang D*. **Lipid-lowering therapy: Guidelines to precision medicine**. Clinica chimica acta; international journal of clinical chemistry 2020; 514:66-73.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33359059

ABSTRACT
Dyslipidemia is correlated with a series of health problems, such as obesity, insulin resistance, and the development of cardiovascular disease (CVD). Currently, accumulating evidence sheds light on the fact that β-hydroxy β-methylglutaryl-CoA reductase inhibitors, named statins, could lower circulating lipid-density lipoprotein cholesterol (LDL-C) and represent a revolution for the prevention of metabolic disorder diseases. In addition, statins remain the cornerstone of LDL-C-lowering treatments, together with ezetimibe and bile acid sequestrants, which are used either in combination with statins or as monotherapies in the case of statin intolerance or side effects. On the other hand, other medicines that reduce circulating LDL-C have also been researched, including inhibitors of protein convertase subtilisin/kexin type 9 (PCSK9). More recently, PCSK9 inhibitors have been approved for the secondary prevention of CVD and for the atherogenic dyslipidemia therapy. Here, we summarize the latest guidelines for the management of dyslipidemia and its relation to CVD, focusing on LDL-C-lowering medicines that are either available in daily clinical practice or under investigation. In addition, we also discuss the "who, when, and how" with respect to treating patients with dyslipidemia according to LDL-C reduction as an individualized clinical precision medicine.

[15] *Bhagavathula AS, Al Matrooshi NO, Clark CCT, Rahmani J*. **Bempedoic Acid and Ezetimibe for the Treatment of Hypercholesterolemia: A Systematic Review and Meta-Analysis of Randomized Phase II/III trials**. Clinical drug investigation 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33368025

ABSTRACT

BACKGROUND AND OBJECTIVE: A limited number of trials have evaluated the efficacy of a fixed-dose combination of bempedoic acid and ezetimibe for the treatment of hypercholesterolemia. The aim of this meta-analysis of existing studies was to evaluate the efficacy and safety of fixed-dose bempedoic acid and ezetimibe combination therapy for the treatment of hypercholesterolemia. METHODS: A systematic literature search was conducted to identify randomized controlled trials (RCTs) comparing bempedoic acid and ezetimibe, versus placebo or ezetimibe alone, to 30 August 2020. A meta-analysis was conducted to investigate the efficacy of bempedoic acid and ezetimibe on lipid parameters and highly sensitive C-reactive protein (hsCRP) levels in patients with hypercholesterolemia or established atherosclerotic cardiovascular disease (ASCVD). Mean differences (MDs) or relative risk (RR) with their corresponding 95% confidence intervals (CIs), using random-effects models, were used to provide pooled estimates. RESULTS: A total of three phase II and III RCTs, comprising 388 patients, of whom 49.2% were treated with bempedoic acid and ezetimibe, and 197 controls, were identified. The duration of treatment was 12 weeks. Bempedoic acid and ezetimibe significantly reduced low-density lipoprotein cholesterol (MD -29.14%, 95% CI -39.52 to -18.76; p < .001), total cholesterol (MD -15.78%, 95% CI -20.84 to -10.72; p = 0.01), non-high-density lipoprotein cholesterol (MD -18.36%, 95% CI -24.60 to -12.12; p = 0.01), and hsCRP levels (MD -30.48%, 95% CI -44.69 to -16.28; p = 0.04). No significant effects on triglycerides (MD -8.35%, 95% CI -16.08 to -0.63; p = 0.72) and improvement in high-density lipoprotein cholesterol (MD 1.63%, 95% CI -4.03 to 7.28; p = 0.92) were observed with the fixed-dose combination therapy. Regarding safety, bempedoic acid and ezetimibe combination was associated with a non-significant increased risk of drug-related adverse events (RR 1.61, 95% CI 0.86-2.35) and overall adverse events (RR 1.16. 95% CI 0.97-1.35); however, the incidence of discontinuation of therapy (RR 0.75, 95% CI 0.35-1.49) was lower. CONCLUSION: This review found bempedoic acid and ezetimibe significantly lowered lipid parameters, attenuated hsCRP levels, and had an acceptable safety profile for the treatment of hypercholesterolemia and ASCVD.

[16] *Powell J, Piszczatoski C*. **Bempedoic Acid: A New Tool in the Battle Against Hyperlipidemia**. Clinical therapeutics 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33384162

ABSTRACT

PURPOSE: This article discusses the pharmacology of bempedoic acid, the trials that led to United States Food and Drug Administration (FDA) approval of its use, and the overall safety and efficacy of this therapy in heterozygous familial hypercholesterolemia, established atherosclerotic cardiovascular disease (ASCVD), and hyperlipidemia. METHODS: A database search of PubMed and ClinicalTrials.gov was conducted for articles published between January 2012 to September 2020 and containing the key words bempedoic acid, ezetimibe, Nexletol and Nexlizet. Trials from the CLEAR series were selected, as they played a pivotal role in the establishment of FDA approval, along with additional trials published after FDA approval, which provided novel evidence on the use of

bempedoic acid in the treatment of hypercholesterolemia. Publications that were not randomized, controlled trials were not included in this review. Only randomized controlled trials in which ezetimibe was used in conjunction with bempedoic acid were included in this review as they were relevant to the new FDA approval of bempedoic acid. FINDINGS: The findings of the present review show that bempedoic acid is both an effective and well-tolerated option for the treatment of hypercholesterolemia when used without ezetimibe in addition to standard therapy. It also appears that the combination with ezetimibe increases the cholesterol-lowering effect more than either agent alone when added to standard therapy. IMPLICATIONS: Hypercholesteremia continues to be a major contributing factor leading to ASCVD. Bempedoic acid is an additional treatment option, along with both statins and diet and exercise, for reducing cholesterol levels and ASCVD events. With the new FDA approval, bempedoic acid may offer an effective therapy for reducing low-density lipoprotein cholesterol in patients at high risk for cardiovascular events due to established ASCVD or heterozygous familial hypercholesterolemia.

[17] *Shehab A, Elnour AA, Bhagavathula AS et al.* **A multicenter prospective hospital-based cohort study on the efficacy and safety of pitavastatin**. Current diabetes reviews 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33371852

ABSTRACT

AIMS: We aim to investigate the efficacy and safety of pitavastatin 4 mg in a population of people living in the United Arab Emirates (UAE). BACKGROUND: Pitavastatin is a member of the HMG-CoA reductase inhibitors family which was approved for use in adult subjects with primary hyperlipidemia or mixed dyslipidemia. To date, no published studies have assessed the efficacy and safety of pitavastatin in the United Arab Emirates. OBJECTIVE: The main objective of the current study was to investigate the efficacy and safety of pitavastatin in subjects with dyslipidemia for primary prevention of cardiovascular diseases based on total cardiovascular risk. METHODS: This was a multicentre (four private hospitals) prospective cohort study to analyze data on the use of pitavastatin for dyslipidemia in adult outpatients in Abu Dhabi and Dubai emirates, United Arab Emirates. We have followed-up the clinical profiles of subjects in four hospitals for six-weeks during the period from June 2015 to June 2017. Efficacy was based on the evaluation of the mean (± standard deviation) change in low-density lipoprotein cholesterol between baseline and week six after the initiation of pitavastatin therapy. Safety was reported as the incidence of adverse events occurred with the use of pitavastatin and the development of new-onset diabetes. RESULTS: A total of 400 subjects who were receiving pitavastatin 4 mg were included. The mean age of subjects was 50.7 ±10.8 years, of these 79.0% were males. At the baseline, the mean level of total cholesterol was 185.4 ±41.5 mg/dL, low density lipoprotein was 154.9 ±48.55 mg/dL, high-density lipoprotein cholesterol was 40.5 ±11.23 mg/dL and fasting blood glucose was 115.0 (±16.63) mg/dl. At the end of six weeks, low density lipoprotein levels significantly decreased to 112.09 ±41.90 mg/dl (standard mean difference [SMD] (-42.8%), 95% CI: -42.88 [-49.17 to -36.58] mg/dl, P <0.001), while high density lipoprotein levels improved (SMD, 95% CI: 1.77% [0.25 to 3.28] mg/dl, P <0.022). There were 55 subjects (13.7%) reported various adverse events such as myalgia (7.5%), sleep disorders (2.5%), and myopathy (2.2%). Furthermore, 4 (1.0%) have had developed new-onset diabetes post six-weeks of initiation of pitavastatin therapy. CONCLUSION: Pitavastatin 4 mg had howed robust efficacy in reducing LDL-C levels and improving HDL-C levels in subjects with dyslipidemias. The use of pitavastatin was

associated with a low discontinuation rate, fewer adverse events, and very limited cases of new-onset diabetes.

[18] *Meroni A, Muirhead RP, Atkinson FS et al.* **Is a Higher Protein-Lower Glycemic Index Diet More Nutritious Than a Conventional Diet? A PREVIEW Sub-study**. Front Nutr 2020; 7:603801.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33365325

ABSTRACT

High protein diets and low glycemic index (GI) diets have been associated with improved diet quality. We compared the changes in nutrient intakes of individuals at high risk of developing type-2 diabetes over 3 y who followed either a higher protein-lower GI diet (HPLG) or a conventional moderate protein-moderate GI diet (MPMG). This post hoc analysis included 161 participants with overweight and pre-diabetes from the Australian cohort of the PREVIEW study (clinical trial registered in https://www.clinicaltrials.gov/ct2/show/NCT01777893?term=NCT01777893&draw=2&rank=1) who were randomly assigned to a HPLG diet (25% energy from protein, dietary GI ≤ 50, n = 85) or a MPMG diet (15% energy from protein, dietary GI ≥ 56, n = 76). Food records were collected at 0-mo (baseline) and at 6-, 12-, 24-, and 36-mo (dietary intervention period). Linear mixed models were used to compare the differences in total energy, macro- and micronutrients, dietary GI, glycemic load (GL) and body weight between the two diet groups at the 4 dietary intervention time points. At 3 y, 74% participants from the HPLG diet and 74% participants from the MPMG diet completed the trial. The HPLG group showed significantly higher protein intake and lower dietary GI and GL than the MPMG group (group fixed effect $P < 0.001$ for all three parameters). By 6-, 12-, 24-, and 36-mo there was a 3.0, 2.7, 2.2, and 1.4% point difference in protein intake and 6.2, 4.1, 4.8, and 3.9 GI unit difference between the groups. The intake of energy and saturated fat decreased (mostly in the first 6-mo), while the intake of dietary fiber increased (from mo-0 to mo-12 only) in both diets, with no significant differences between the diets. The dietary intakes of zinc (group fixed effect $P = 0.05$), selenium ($P = 0.01$), niacin ($P = 0.01$), vitamin B12 ($P = 0.01$) and dietary cholesterol (group by time fixed effect $P = 0.001$) were higher in the HPLG group than in the MPMG group. Despite both diets being designed to be nutritionally complete, a HPLG diet was found to be more nutritious in relation to some micronutrients, but not cholesterol, than a MPMG diet.

[19] *Liu J, Wu J, Li L et al.* **The Role of Exosomal Non-Coding RNAs in Coronary Artery Disease**. Frontiers in pharmacology 2020; 11:603104.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33363474

ABSTRACT

Cardiovascular disease (CVD) remains the leading cause of morbidity and mortality worldwide. Atherosclerosis (AS) is a major cause of CVD. Oxidative stress, endothelial dysfunction, and inflammation are key factors involved in the development and progression of AS. Exosomes are nano-sized vesicles secreted into the extracellular space by most types of cells, and are ideal substances for the transmission and integration of signals between cells. Cells can selectively encapsulate biologically active substances, such as lipids, proteins and RNA in exosomes and act through paracrine mechanisms. Non-coding RNAs (ncRNAs) are important for communication between cells. They can reach the recipient cells through exosomes, causing phenotypic changes and playing a molecular regulatory role in cell function. Elucidating their molecular mechanisms can help identify therapeutic targets or strategies for CVD. Coronary artery disease (CAD) is the most

important disease in CVD. Here, we review the role and the regulatory mechanism of exosomal ncRNAs in the pathophysiology of CAD, as well as the potential contribution of exosomal ncRNA to diagnosis and treatment of CAD.

[20] *Schlüter KD, Wolf A, Schreckenberg R*. **Coming Back to Physiology: Extra Hepatic Functions of Proprotein Convertase Subtilisin/Kexin Type 9**. Front Physiol 2020; 11:598649.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33364976

ABSTRACT

Neuronal apoptosis regulated convertase-1 (NARC-1), now mostly known as proprotein convertase subtilisin/kexin type 9 (PCSK9), has received a lot of attention due to the fact that it is a key regulator of the low-density lipoprotein (LDL) receptor (LDL-R) and is therefore involved in hepatic LDL clearance. Within a few years, therapies targeting PCSK9 have reached clinical practice and they offer an additional tool to reduce blood cholesterol concentrations. However, PCSK9 is almost ubiquitously expressed in the body but has less well-understood functions and target proteins in extra hepatic tissues. As such, PCSK9 is involved in the regulation of neuronal survival and protein degradation, it affects the expression of the epithelial sodium channel (ENaC) in the kidney, it interacts with white blood cells and with cells of the vascular wall, and it modifies contractile activity of cardiomyocytes, and contributes to the regulation of cholesterol uptake in the intestine. Moreover, under stress conditions, signals from the kidney and heart can affect hepatic expression and thereby the plasma concentration of PCSK9 which then in turn can affect other target organs. Therefore, there is an intense relationship between the local (autocrine) and systemic (endocrine) effects of PCSK9. Although, PCSK9 has been recognized as a ubiquitously expressed modifier of cellular function and signaling molecules, its physiological role in different organs is not well-understood. The current review summarizes these findings.

[21] *Mostafa TM, Hegazy SK, Elshebini EM et al.* **A comparative study on the anti-inflammatory effect of angiotensin-receptor blockers & statins on rheumatoid arthritis disease activity**. The Indian journal of medical research 2020; 152:393-400.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33380704

ABSTRACT

BACKGROUND & OBJECTIVES: : Rheumatoid artherits (RA) is a refractory disease and the imbalance between pro- and anti-inflammatory cytokines in favor of pro-inflammatory cytokines has been implicated in pathogenesis of RA. In this context, the aim of the present study was to compare the anti-inflammatory and antioxidant effects of candesartan, an angiotensin-receptor blocker, and atorvastatin in RA patients. METHODS: : In this single-blinded parallel randomized placebo controlled study, the patients recruited between December 2017 and May 2018 were categorized into three groups: group 1 included 15 RA patients who served as control group and received traditional therapy (+ placebo); group 2 included 15 RA patients who received traditional therapy + candesartan (8 mg/day); and group 3 included 15 patients who received traditional therapy + atorvastatin (20 mg/day) for three months. Clinical status in RA patients was evaluated by Disease Activity Score 28 (DAS28), Health Assessment Questionnaire-Disability Index (HAQ-DI) and morning stiffness before and three months after treatment. All groups were subjected to biochemical analysis of C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), tumour necrosis factor-alpha (TNF-α), interleukin-1beta (IL-1β) and malondialdehyde (MDA) before and three months after treatment. RESULTS: : Both

candesartan and atorvastatin treated groups showed significant decrease in serum levels IL-1β and TNF-α, acute-phase reactants (CRP and ESR), number of swollen joint and patient global assessment. This was also associated with improvement in disease activity and quality of life regarding DAS28 and HAQ-DI as compared to baseline data and the control group. Atorvastatin group showed significant decrease in the serum level of oxidative stress marker (MDA). INTERPRETATION & CONCLUSIONS: : Both candesartan and atorvastatin showed anti-inflammatory effect and immunomodulatory effects leading to improvement in clinical status and disease activity in RA patients. However, atorvastatin was superior to candesartan through its anti-oxidant effect.

[22] *Teklu M, Zhou W, Kapoor P et al.* **Metabolic Syndrome and its Factors are Associated with Non-Calcified Coronary Plaque Burden in Psoriasis: An Observational Cohort Study**. Journal of the American Academy of Dermatology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33383084
ABSTRACT
BACKGROUND: Psoriasis is associated with a heightened risk of cardiovascular disease (CVD) and higher prevalence of metabolic syndrome (MetSyn) and its individual components. OBJECTIVE: Investigate the impact of MetSyn and its components on early coronary artery disease assessed as non-calcified coronary burden (NCB) by coronary computed tomography angiography (CCTA) in psoriasis. METHODS: This cross-sectional study consisted of 260 participants with psoriasis and CCTA results. MetSyn was defined according to the harmonized International Diabetes Federation criteria. RESULTS: Of the 260 participants, 80 had MetSyn (31%). The MetSyn group had a higher burden of cardiometabolic disease, systemic inflammation, NCB, and high-risk plaque. After adjusting for Framingham risk score, lipid-lowering therapy, and biologic use, MetSyn (β=0.31; p<.001) and its individual components of waist circumference (β=0.33; p<.001), triglycerides (β=0.17; p=.005), blood pressure (β=0.18; p=.005) and fasting glucose (β=0.17; p=.009) associated with NCB. After adjusting for all other MetSyn factors, blood pressure and waist circumference remained significantly associated with NCB. LIMITATIONS: Observational nature with limited ability to control for confounders. CONCLUSIONS: In psoriasis, those with MetSyn had more CVD risk factors, systemic inflammation, and coronary plaque burden. Efforts to increase MetSyn awareness in psoriasis should be undertaken to reduce the heightened CVD risk.

[23] *Dixon DL, Saseen JJ*. **Pharmacist-administered long-acting injectable PCSK9 service: A solution to improve patient access and adherence**. Journal of the American Pharmacists Association : JAPhA 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33384242
ABSTRACT
In 2015, 2 proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, alirocumab and evolocumab, were approved by the Food and Drug Administration (FDA). Both therapies reduce low-density lipoprotein cholesterol (LDL-C) by approximately 60% and reduce atherosclerotic cardiovascular disease (ASCVD) risk in patients with established ASCVD when added to background statin therapy. The initial cost of these medications was approximately $15,000 per year, which made them largely cost-prohibitive for many patients and the overall health care system. In recent years, the cost of both agents has been reduced by 60%, and they are no longer only available through

specialty pharmacies. In addition, a third PCSK9-modulating therapy, inclisiran, is nearing FDA approval. Ongoing inclisiran therapy only requires biannual subcutaneous administration and achieves LDL-C reductions of approximately 50%. As the use of PCSK9-modulating therapies increases, models that improve adherence and persistence over time will be critical to ensure patient access and maximize their value. Community pharmacists can play an important role helping patients not only obtain access to these therapies by navigating previous authorization requests but also adhere to therapy by offering administration. Community pharmacists can also provide therapeutic monitoring using point-of-care lipid testing to ensure efficacy over time. Such a service could potentially be sustained through reimbursement for administration and point-of-care lipid testing. Given the cost of these therapies, innovative models involving community pharmacists will be necessary to ensure patient access to these preventive therapies and minimize overall costs to the health care system.

[24] *Conti P, Caraffa A, Gallenga CE et al.* **The British variant of the new coronavirus-19 (Sars-Cov-2) should not create a vaccine problem**. Journal of biological regulators and homeostatic agents 2021; 35.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33377359

ABSTRACT
Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a highly contagious virus that infects humans and a number of animal species causing coronavirus disease-19 (COVID-19), a respiratory distress syndrome which has provoked a global pandemic and a serious health crisis in most countries across our planet. COVID-19 inflammation is mediated by IL-1, a disease that can cause symptoms such as fever, cough, lung inflammation, thrombosis, stroke, renal failure and headache, to name a few. Strategies that inhibit IL-1 are certainly helpful in COVID-19 and can represent one of the therapeutic options. However, until now, COVID-19 therapy has been scarce and, in many cases, ineffective, since there are no specific drugs other than the vaccine that can solve this serious health problem. Messenger RNA (mRNA) vaccines which are the newest approach, are already available and will certainly meet the many expectations that the population is waiting for. mRNA vaccines, coated with protected soft fatty lipids, use genetic mRNA (plus various inactive excipients) to make a piece of the coronavirus spike protein, which will instruct the immune system to produce specific antibodies. The soft fatty lipids allow the entry of mRNA into cells where it is absorbed into the cytoplasm and initiates the synthesis of the spike protein. In addition, vaccination also activates T cells that help the immune system respond to further exposure to the coronavirus. mRNA induces the synthesis of antigens of SARS-CoV-2 virus which stimulate the antibody response of the vaccinated person with the production of neutralizing antibodies. The new variant of the coronavirus-19 has been detected in the UK where, at the moment, the London government has imposed a lockdown with restrictions on international movements. The virus variant had already infected 1/4 of the total cases and in December 2020, it reached 2/3 of those infected in the UK. It has been noted that the spreading rate of the British variant could be greater than 70% of cases compared to the normal SARS-CoV-2 virus, with an R index growth of 0.4. Recent studies suggest that coronavirus-19 variation occurs at the level N501Y of the spike protein and involves 23 separate mutations on the spike, 17 of which are linked to the virus proteins, thus giving specific characteristics to the virus. In general, coronaviruses undergo many mutations that are often not decisive for their biological behavior and does not significantly alter the structure and the components of the virus. This

phenomenon also occurs in SARS-CoV-2. It is highly probable that the variants recently described in the UK will not hinder vaccine-induced immunity. In fact, the variant will not break the vaccine although it may have some chance of making it a little less effective. Therefore, it is pertinent to think that the vaccine will work against the SARS-CoV-2 variant as well. In today's pandemic, the D614G mutation of the amino acid of corronavirus-19, which emerged in Europe in February 2020 is the most frequent form and causes high viral growth. The previously infrequent D614G mutation is now globally dominant. This variant, which is being tested by many international laboratories, is rapidly spreading across the countries and a series of vaccinated subjects are testing to see if their antibodies can neutralize the new variant of SARS-CoV-2. This variant has a very high viral growth and is less detectable with the RT-PCR technique in the laboratory. It has been reported that the British variant that increases viral load does not cause more severe effects in the respiratory tract and lung disease, therefore, it is certain that the variant is growing rapidly and must be kept under control; for this reason, laboratory data is expected impatiently. The study on the many variants that coronavirus-19 presents is very interesting and complete and clearer data on this topic will be ready in the near future. In addition, it is still unclear whether the different variants discovered in many countries, including Africa, share the same spike protein mutation and therefore, this is another study to elaborate on. In order to be certain and to not have unexpected surprises, we need to reduce the spread and the transmission speed of viral variants that could appear around the world, creating new pandemics. For this reason, the scientific community is on the alert since laboratory tests on serum antibodies from COVID-19 survivors have been reported to be less effective in attacking the variant. In light of the above, the scientific community must be on the alert as larger variants of the spike protein could escape vaccine-induced antibodies, which for now are of great help to the community and can save millions of lives. Deepening the study of spike protein mutations will help to better understand how to combat coronavirus-19 and its variants.

[25] *Ben Braiek A, Chahed H, Dumont F et al.* **Identification of biomarker panels as predictors of severity in coronary artery disease**. Journal of cellular and molecular medicine 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33381894

ABSTRACT

Matrix metalloproteinases (MMPs) are implicated in atherosclerotic plaque rupture and recondition. Specific tissue inhibitors (TIMPs) control MMP functions. Both MMPs and TIMPs are potential biomarkers of plaque instability. Elevated Apo-CII and CIII and Apo-E levels are recognized as cardiovascular disease risk factors. We aimed to establish the best blood biomarker panel to evaluate the coronary artery disease (CAD) severity. Plasma levels of MMP-3 and MMP-9, TIMP-1 and TIMP-2, Apo-CII, Apo-CIII and Apo-E were measured in 472 patients with CAD evaluated by coronary angiography and electrocardiography, and in 285 healthy controls. MMP-3 and MMP-9 plasma levels in CAD patients were significantly increased ($P < 0.001$) compared to controls (3.54- and 3.81-fold, respectively). Furthermore, these increments are modulated by CAD severity as well as for Apo-CII and Apo-CIII levels ($P < 0.001$). TIMPs levels were decreased in CAD versus controls ($P < 0.001$) and in inverse correlation to MMPs. Standard ROC curve approach showed the importance of panels of biomarkers, including MMP-3, MMP-9, TIMP-1, TIMP-2, Apo-CII and Apo-CIII, for disease aggravation diagnosis. A high area under curve (AUC) value (0.995) was reached for the association of MMP-9, TIMP-2 and Apo-CIII. The unbalance between MMPs and TIMPs in vascular wall and dyslipidaemia creates favourable conditions for plaque disruption. Our study suggests that the

combination of MMP-9, TIMP-2 and Apo-CIII values ('CAD aggravation panel') characterizes the severity of CAD, that is electrophysiological state, number of involved vessels, stent disposal and type of stent.

[26] *Jung YY, Ko JH, Um JY et al.* **LDL cholesterol promotes the proliferation of prostate and pancreatic cancer cells by activating the STAT3 pathway**. Journal of cellular physiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33368314

ABSTRACT

Hypercholesterolemia has been found to be closely linked with a significant increase in both cancer incidence and mortality. However, the exact correlation between serum cholesterol levels and cancer has not been completely deciphered. Here we analyzed the effect of low-density lipoprotein (LDL) cholesterol on prostate and pancreatic cancer cells. We noted that LDL induced a substantial STAT3 activation and JAK1, JAK2, Src activation in diverse prostate and pancreatic tumor cells. Moreover, LDL promoted cancer cell proliferation, migration, and invasion as well as upregulated the expression of diverse oncogenic gene products. However, deletion of LDL-activated STAT3 in LNCaP and PANC-1 cells and reduced LDL-induced cell viability. Simvastatin (SV) treatment also alleviated LDL-induced cell viability and migration ability in both the prostate and pancreatic tumor cells. These results demonstrate that LDL-induced STAT3 activation may exert a profound effect on the proliferation and survival of tumor cells.

[27] *Mickiewicz A, Marlega J, Kuchta A et al.* **Cardiovascular events in patients with familial hypercholesterolemia and hyperlipoproteinaemia (a): Indications for lipoprotein apheresis in Poland**. Journal of clinical apheresis 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33386762

ABSTRACT

BACKGROUND: Lipoprotein apheresis (LA) is a safe method of reducing atherogenic lipoproteins and improving cardiovascular (CV) outcomes. We aimed to assess the reductions in low-density lipoprotein cholesterol (LDL-C) and lipoprotein (a) [Lp(a)] levels in patients undergoing regular LA therapy and to evaluate its influence on the incidence rate of adverse cardiac and vascular events (ACVE) and major adverse cardiac events (MACE). METHODS: A longitudinal study in Poland evaluated the prospective and retrospective observational data of 23 patients with hyperlipoproteinaemia (a) [hyper-Lp(a)] and familial hypercholesterolemia (FH), undergoing 1014 LA sessions between 2013 and 2020. Their pre- and post-apheresis LDL-C and Lp(a) levels were assessed to calculate the acute percent reductions. The time period used to evaluate annual rates of ACVE and MACE before and after initiation of LA was matched in each patient. RESULTS: The pre-apheresis LDL-C and Lp(a) concentrations were 155 (107-228) (mg/dL) (median and interquartile range) and 0.56 (0.14-1.37) (g/L), respectively. LA therapy resulted in a reduction of LDL-C to 50 (30-73.5) (mg/dL) and of Lp(a) to 0.13 (0.05-0.34) (g/L), representing a percent reduction of 70.0% and 72.7% for LDL-C and Lp(a), respectively. We found a significant reduction in the annual rate of ACVE (0.365[0.0-0.585] vs (0.0[0.0-0.265]; P = .047) and MACE (0.365[0.0-0.585] vs 0.0[0.0-0.265]; P = .031). CONCLUSIONS: The findings of our study indicate that LA treatment in patients with hyperlipoproteinaemia (a) and FH on maximally tolerated lipid lowering therapies leads to a substantial reduction in LDL-C and Lp(a) concentrations and lowers CV event rates in Polish patients.

[28] *Hovland A, Narverud I, Lie Øyri LK et al.* **Subjects with familial hypercholesterolemia have lower aortic valve area and higher levels of inflammatory biomarkers**. Journal of clinical lipidology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33358307

ABSTRACT
BACKGROUND: Reduction of the aortic valve area (AVA) may lead to aortic valve stenosis with considerable impact on morbidity and mortality if not identified and treated. Lipoprotein (a) [Lp(a)] and also inflammatory biomarkers, including platelet derived biomarkers, have been considered risk factor for aortic stenosis; however, the association between Lp(a), inflammatory biomarkers and AVA among patients with familial hypercholesterolemia (FH) is not clear. OBJECTIVE: We aimed to investigate the relation between concentration of Lp(a), measurements of the aortic valve including velocities and valve area and circulating inflammatory biomarkers in adult FH subjects and controls. METHODS: In this cross-sectional study aortic valve measures were examined by cardiac ultrasound and inflammatory markers were analyzed in non-fasting blood samples. The study participants were 64 FH subjects with high (n = 29) or low (n = 35) Lp(a), and 14 healthy controls. RESULTS: Aortic valve peak velocity was higher (p = 0.02), and AVA was lower (p = 0.04) in the FH patients compared to controls; however, when performing multivariable linear regression, there were no significant differences. Furthermore, there were no significant differences between the high and low FH Lp(a) groups regarding the aortic valve. FH subjects had higher levels of platelet-derived markers CD40L, PF4, NAP2 and RANTES compared to controls ($0.003 \leq P \leq 0.03$). This result persisted after multiple linear regression. CONCLUSIONS: Middle-aged, intensively treated FH subjects have higher aortic valve velocity, lower AVA, and higher levels of the platelet-derived markers CD40L, PF4, NAP2 and RANTES compared to healthy control subjects. The aortic valve findings were not significant after multiple linear regression, whereas the higher levels of platelet-derived markers were maintained.

[29] *Ceballos-Macías JJ, Lara-Sánchez C, Flores-Real J et al.* **PCSK-9 Inhibitors in a Real-World Setting and a Comparison Between Alirocumab and Evolocumab in Heterozygous FH Patients**. Journal of the Endocrine Society 2021; 5:bvaa180.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33367195

ABSTRACT
A real-world setting study of familial hypercholesterolemia (FH) patients who received Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors in a specialized referral center in Mexico City. Ten patients between the ages of 18 and 70 years, with a diagnosis of FH according to Dutch Lipid Clinic Network (DLCN) criteria, with failure to achieve their Low-density lipoprotein Cholesterol (LDL-C) goals, and with standard therapy between 2016 and 2017 enrolled in a simple randomization in which a group of 5 participants received alirocumab (75 mg every 2 weeks) and the remaining 5 patients received evolocumab (140 mg every 2 weeks). Comparative analysis was made, analyzing the means of LDL at baseline at 4, 6, and 12 weeks. The evolocumab group had an average initial LDL-C of 277 mg/dL, which, after 12 weeks of treatment, was significantly reduced to 116 mg/dL; P = 0.04 (95% confidence interval [CI]: 11.5-310.9). The alirocumab group with a mean initial LDL-C of 229 mg/dL showed a reduction of LDL-C levels at 12 weeks of treatment to 80 mg/dL; P = 0.008 (95% CI: 63.8-233.7). In conclusion, PCSK9 inhibitors are an excellent treatment option in patients with FH who do not reach their LDL-C goals with standard therapy or due to intolerance to the standard therapy. There is no difference in the lipid-lowering effect between both PSCK9 inhibitors.

[30] *Busik JV*. **Lipid metabolism dysregulation in diabetic retinopathy**. Journal of lipid research 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33361283
ABSTRACT
Lipid metabolic abnormalities have emerged as potential risk factors for the development and progression of diabetic complications, including diabetic retinopathy (DR). This review article provides an overview of the results of clinical trials evaluating the potential benefits of lipid lowering drugs, such as fibrates, omega 3 fatty acids, and statins, for the prevention and treatment of DR. Although several clinical trials demonstrated that treatment with fibrates leads to improvement of DR, there is a dissociation between the protective effects of fibrates in the retina, and the intended blood lipid classes, including plasma triglycerides, total cholesterol or HDL/LDL cholesterol ratio. Guided by these findings, plasma lipid and lipoprotein-independent mechanisms are addressed based on clinical, cell culture and animal model studies. Potential retinal-specific effects of fatty acids oxidation products, cholesterol, and ceramide, as well as lipid independent effects of PPAR alpha activation are summarized based on current literature. Overall, this review highlights promising potential of lipid-based treatment strategies further enhanced by the new knowledge of intra-retinal lipids and lipoproteins in DR.

[31] *Guasch-Ferré M, Hernández-Alonso P, Drouin-Chartier JP et al.* **Walnut Consumption, Plasma Metabolomics, and Risk of Type 2 Diabetes and Cardiovascular Disease**. The Journal of nutrition 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33382410
ABSTRACT
BACKGROUND: Walnut consumption is associated with lower risk of type 2 diabetes (T2D) and cardiovascular disease (CVD). However, it is unknown whether plasma metabolites related to walnut consumption are also associated with lower risk of cardiometabolic diseases. OBJECTIVES: The study aimed to identify plasma metabolites associated with walnut consumption and evaluate the prospective associations between the identified profile and risk of T2D and CVD. METHODS: The discovery population included 1833 participants at high cardiovascular risk from the PREvención con DIeta MEDiterránea (PREDIMED) study with available metabolomics data at baseline. The study population included 57% women (baseline mean BMI (in kg/m2): 29.9; mean age: 67 y). A total of 1522 participants also had available metabolomics data at year 1 and were used as the internal validation population. Plasma metabolomics analyses were performed using LC-MS. Cross-sectional associations between 385 known metabolites and walnut consumption were assessed using elastic net continuous regression analysis. A 10-cross-validation (CV) procedure was used, and Pearson correlation coefficients were assessed between metabolite weighted models and self-reported walnut consumption in each pair of training-validation data sets within the discovery population. We further estimated the prospective associations between the identified metabolite profile and incident T2D and CVD using multivariable Cox regression models. RESULTS: A total of 19 metabolites were significantly associated with walnut consumption, including lipids, purines, acylcarnitines, and amino acids. Ten-CV Pearson correlation coefficients between self-reported walnut consumption and the plasma metabolite profile were 0.16 (95% CI: 0.11, 0.20) in the discovery population and 0.15 (95% CI: 0.10, 0.20) in the validation population. The metabolite profile was inversely associated with T2D

incidence (HR per 1 SD: 0.83; 95% CI: 0.71, 0.97; P = 0.02). For CVD incidence, the HR per 1-SD was 0.71 (95% CI: 0.60, 0.85; P < 0.001). CONCLUSIONS: A metabolite profile including 19 metabolites was associated with walnut consumption and with a lower risk of incident T2D and CVD in a Mediterranean population at high cardiovascular risk.

[32] *Ruggiero E, Di Castelnuovo A, Costanzo S et al.* **Daily Coffee Drinking Is Associated with Lower Risks of Cardiovascular and Total Mortality in a General Italian Population: Results from the Moli-sani Study**. The Journal of nutrition 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33382422
ABSTRACT
BACKGROUND: An inverse relationship between coffee intake and mortality has been observed in several population cohorts, but rarely within Mediterranean countries. Moreover, the biological pathways mediating such an association remain unclear. OBJECTIVES: We assessed the associations between coffee consumption and total and cause-specific mortality and examined the mediating roles of N-terminal pro B-type natriuretic peptide (NTproBNP), high-sensitivity Troponin I, blood glucose, lipid metabolism, and selected biomarkers of inflammation and renal function. METHODS: We longitudinally analyzed data on 20,487 men and women (35-94 years old at baseline) in the Moli-sani Study, a prospective cohort established in 2005-2010. Individuals were free from cardiovascular disease (CVD) and cancer and were followed-up for a median of 8.3 years. Dietary data were collected by a 188-item semi-quantitative FFQ. Coffee intake was standardized to a 30-mL Italian espresso cup size. HRs with 95% CIs were calculated by multivariable Cox regression. RESULTS: In comparison with no/rare coffee consumption (up to 1 cup/d), HRs for all-cause mortality across categories of coffee consumption (>1 to ≤2, >2 to ≤3, >3 to ≤4 and >4 cups/d) were 0.79 (95% CI, 0.65-0.95), 0.84 (95% CI, 0.69-1.03), 0.72 (95% CI, 0.57-0.92), and 0.85 (95% CI, 0.62-1.12), respectively. For CVD mortality, a nonlinear (P for non-linearity = 0.021) J-shaped association was found (magnitude of the relative reduction = 37%; nadir at 3-4 cups/d). Circulating levels of NTproBNP explained up to 26.4% of the association between coffee and all-cause mortality, while systolic blood pressure was likely to be on the pathway between coffee and CVD mortality, although to a lesser extent. CONCLUSIONS: In this large cohort of Italian adults, moderate consumption (3-4 cups/d) of Italian-style coffee was associated with lower risks of all-cause and, specifically, of CVD mortality. Among the known biomarkers investigated here, NTproBNP likely mediates the relationship between coffee intake and all-cause mortality.

[33] *Yilmaz E, Akay KH*. **The Efficacy of Colchicine on Carotid Intima-Media Thickness: A Prospective Comparative Study**. Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association 2020; 30:105580.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33387888
ABSTRACT
OBJECTIVES: Inflammation plays an important role in the development of atherosclerotic vascular disease, which is the leading cause of morbidity and mortality in the adult population. Several clinical trials have shown that suppression of the inflammatory response can delay or decrease the atherosclerotic process. The aim of this study was to investigate carotid intima-media thickness (CIMT) between patients with chronic disease history plus gout using colchicine and patients with cardiovascular risk factors. MATERIALS AND METHODS: In total, 102 patients (85 female, 17 male)

were included. There were two groups in the study: Group 1 - patients with chronic diseases including cardiovascular risk factors plus gout using colchicine (0,5 mg twice a day); and Group 2 - patients with chronic diseases including cardiovascular risk factors only. All patients underwent ultrasonography for the measurement of CIMT. Additionally, the serum concentrations of C-reactive protein (CRP) and the levels of lipids such as cholesterol, triglyceride, LDL, HDL were measured. RESULTS: The mean age of patients was 62.35±6.68 years and 64.27±5.32 years in Group 1 and Group 2, respectively. There was also no statistically significant difference in the levels of lipids between groups ($p>0.05$). The value of CIMT and CRP in Group 1 and Group 2 were 0.98±0.20 and 0.26±0.14, 1.18±0.15 and 0.58±0.42, respectively. There was a statistically significant difference between groups ($p<0.05$). The colchicine group was found to have a statistically significant lowering of CIMT and CRP compared to the non-colchicine group. CONCLUSIONS: It appears that colchicine in addition to statins and other standard treatments is an effective treatment for the interception of cardiovascular and cerebrovascular events in patients with cardiovascular risk factors.

[34] *Fedak A, Chrzan R, Chukwu O, Urbanik A*. **Ultrasound methods of imaging atherosclerotic plaque in carotid arteries: examinations using contrast agents**. Journal of ultrasonography 2020; 20:e191-e200.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33365156
ABSTRACT
The primary technique for detecting the presence and monitoring the development of carotid atherosclerotic plaque is ultrasound. The development of ultrasound techniques has made it possible to precisely visualise not only blood flow, but also vessel walls, including atherosclerotic plaque. Contrast-enhanced ultrasound examination enables one to make an objective observation of atherosclerotic plaque neovascularisation, clearly indicating active inflammation, which is an inherent feature of vulnerable (unstable) plaque. Depending on the examination method used, it is possible to precisely visualise different components of the plaque and its behaviour during blood flow through the vessel lumen or through the neovessels of the plaque, and, consequently, determine the possible presence of inflammation, which is a defining feature of plaque stability. The full utilisation of physical phenomena that underlie contrast-enhanced ultrasound will bring further enormous progress of diagnostic and probably also therapeutic methods for carotid atherosclerosis. The selection of the right examination method significantly accelerates diagnosis and adequate classification of plaque, and makes it possible to monitor the progression of atherosclerosis. However, one needs to bear in mind that ultrasound remains a very subjective method. The success of contrast-enhanced ultrasound also depends on the skills and experience of the examiner. Current attempts at increasing the objectivity of contrast-enhanced ultrasound examination using artificial intelligence will make it possible in the future to make a definitive evaluation of atherosclerotic plaque stability. This will allow one to assess the risk of ischaemic stroke adequately.

[35] *Saeidifard F, Medina-Inojosa JR, Supervia M et al.* **The Effect of Replacing Sitting With Standing on Cardiovascular Risk Factors: A Systematic Review and Meta-analysis**. Mayo Clinic proceedings. Innovations, quality & outcomes 2020; 4:611-626.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33367205
ABSTRACT

OBJECTIVE: To investigate the effect of replacing sitting with standing on cardiovascular risk factors tested in clinical trials. METHODS: We searched databases from inception up to August 28, 2019, for studies examining the effect of replacing sitting with standing on fasting blood glucose, fasting insulin, and lipid levels; blood pressure; body fat mass; weight; and waist circumference in healthy adults. Differences in mean ± SD values were used for pooling the data and calculating the mean differences and CIs. RESULTS: The search found 3507 abstracts. Nine clinical trials (8 randomized and 1 nonrandomized) with 877 (64.4% [n=565] women) participants met all inclusion criteria. The mean ± SD age was 45.34±5.41 years; mean follow-up was 3.81 months, and mean difference in standing time between the intervention and control groups was 1.33 hours per day. The follow-up fasting blood glucose and body fat mass values were slightly but significantly lower than baseline records in the intervention groups compared with control groups (-2.53; 95% CI, -4.27 to -0.79 mg/dL; and -0.75; 95% CI, -0.91 to -0.59 kg). The analysis for fasting insulin levels, lipid levels, blood pressure, weight, and waist circumference revealed no significant differences. CONCLUSION: Replacing sitting with standing can result in very small but statistically significant decreases in fasting blood glucose levels and body fat mass with no significant effect on lipid levels, blood pressure, weight, and waist circumference. Replacing sitting with standing can be used as an adjunctive intervention to decrease the burden of cardiovascular risk factors but cannot be used as an alternative to physical activity to decrease sedentary time.

[36] *Viktorinova A, Fabryova L, Malickova D et al.* **Clinical Utility of the Logarithmically Transformed Ratio of Triglycerides-to- High-Density Lipoprotein Cholesterol and Its Relationship with Other Atherosclerosis-Related Lipid Factors in Type 2 Diabetes**. Metab Syndr Relat Disord 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33373539

ABSTRACT

Background: Elevated triglyceride (TG) levels and reduced high-density lipoprotein-cholesterol (HDL-c) levels indicate lipid abnormalities, but their levels alone do not reflect the actual status of plasma atherogenicity and cardiovascular disease risk (CVD). TG and HDL-c levels directly affect the balance between plasma atherogenic and antiatherogenic factors, as well as values of the atherogenic index of plasma [AIP (logarithmically transformed ratio of TG-to-HDL-c)]. The aim of this study was to evaluate the AIP risk categories (an indicator of plasma atherogenicity) and the relationships of AIP with other atherosclerosis-related lipid parameters in patients with type 2 diabetes mellitus (T2DM) and their potential clinical utility. Methods: Standard lipid profile, AIP, and lipid hydroperoxides (LOOH) were investigated in 124 T2DM outpatients (mean age 52.7 ± 5.9 years) and 61 healthy subjects (mean age 50.9 ± 6.8 years). T2DM patients were subclassified according to the AIP risk category and glycemic control. Results: Higher levels of AIP, LOOH, and TG and lower HDL-c (all $P < 0.0001$) were observed in T2DM patients than in the control group. AIP positively correlated with LOOH, non-HDL-c, and the non-HDL/HDL ratio (all $P < 0.0001$). The TG level was strongly correlated with the LOOH level among T2DM patients ($P < 0.0001$). Conclusions: The close association of AIP with other atherosclerosis-related lipid factors reveals an increased plasma atherogenicity. AIP risk categories indicate the actual status of plasma atherogenicity and identify subjects who are at an increased atherogenic risk and the development of CVD. In this respect, AIP has a promising future in routine clinical practice.

[37] *Gil-Núñez A, Masjuan J, Montaner J et al.* **Proprotein convertase subtilisin/kexin type 9 inhibitors in secondary prevention of vascular events in patients with stroke: Consensus document and practice guidance**. Neurologia 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33358061

ABSTRACT
INTRODUCTION: Patients with history of stroke or transient ischaemic attack present considerable risk of future vascular events. Reducing levels of low-density lipoprotein (LDL) cholesterol decreases the incidence of new vascular events, although in a substantial number of patients, the currently available lipid-lowering therapies fail to achieve the therapeutic goals recommended in clinical guidelines. The aim of this consensus statement is to provide updated information on the role of the proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors alirocumab and evolocumab in the secondary prevention of vascular events in patients with history of ischaemic stroke. METHODS: A literature review was performed to identify the main evidence on the use of PCSK9 inhibitors in these patients and the recommended therapeutic targets of LDL cholesterol. The results were discussed in 2 consensus meetings that constituted the basis for the drafting of the document. CONCLUSIONS: PCSK9 inhibitors are effective in reducing vascular risk in secondary prevention; evolocumab specifically has achieved this reduction in patients with history of ischaemic stroke. Moreover, both alirocumab and evolocumab present good safety profiles, even in patients achieving LDL cholesterol levels <20 mg/dL, and no signs of cognitive impairment have been observed in patients treated with evolocumab who achieved very low levels of LDL cholesterol. In the light of this evidence, we provide practical recommendations about the use of PCSK9 inhibitors in secondary prevention of vascular events in patients with history of ischaemic stroke and follow-up of these patients.

[38] *Pawlos A, Broncel M, Wlazłowska E et al.* **Cardiovascular risk and response to lipid lowering therapy in patients with HIV infection according to different recommendations**. PloS one 2020; 15:e0244675.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33373417

ABSTRACT
BACKGROUND: HIV patients are at increased cardiovascular risk while available European cardiovascular recommendations are ambiguous. METHODS: Retrospective analysis of 389 HIV-patients was conducted. Cardiovascular risk was determined by D:A:D, Framingham and SCORE scales. Patients were divided into risk groups as recommended by EACS 2019, PTN AIDS 2019 and ESC/EAS 2019 Guidelines and hypolipemic treatment was evaluated. RESULTS: In total, 389 HIV-positive patients took part in the study, most of whom were men (n = 312, 80.4%), mean age 41.69±10years. Mean lipid levels among all HIV patients: Tch:177.2±36mg/dl, HDL:48.9±18mg/dl, LDL:103.8±31mg/dl, TG:143.3±81mg/dl, AIP:0.45±0.3, non-HDL:129.2±36 mg/dl. Most of the participants (n = 360, 92.5%) were assigned to the high cardiovascular risk group according to ESC/EAS and PTN AIDS guidelines. The achievement of therapeutic LDLs according to ESC/EAS was 10.3% for those at very high cardiovascular risk (8.7% on lipid lowering treatment vs. 16.7% without hypolipemic drugs) and 12.0% (5.8% treated vs. 13.6% untreated) at high cardiovascular risk; according to PTN AIDS,17.2% achievement was noted by the very high-risk group (13% treated vs. 33.3% untreated), and 45.9% for the high-risk group (37.7% treated vs. 48.0% untreated); according to EACS Guidelines, 2.5% achievement in secondary prevention (3.8% treatedvs. 0% untreated) and 24.7% in primary prevention (22.2% treated vs. 26.1% untreated). Mean doses of statins were

8.75mg±6mg (Rosuvastatin) and 22.35±19mg (Atorvastatin). CONCLUSIONS: The achievement of therapeutic LDLs by all recommendations is unsatisfactory, and generally worse in patients on lipid lowering therapy. Hypolipemic treatment of our HIV patients is based on low doses of statins, even in secondary prevention.

[39] *Tesfa E, Nibret E, Munshea A*. **Maternal lipid profile and risk of pre-eclampsia in African pregnant women: A systematic review and meta-analysis**. PloS one 2020; 15:e0243538.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33362205

ABSTRACT

INTRODUCTION: Some studies have reported the association between maternal serum lipid profile abnormalities and pre-eclampsia. However, many studies have reported controversial results. Hence, this systematic review and meta-analysis was planned to generate summarized evidence on the association between maternal serum lipid profiles and pre-eclampsia in African women. METHODS: Four electronic databases such as; PubMed, Hinari, Google Scholar, and African Journals Online were searched for studies published in English. Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instrument and Newcastle-Ottawa Scale were used for data extraction and quality assessment of the included studies. The meta- regression analysis was performed by Stata 14 software. The standardized mean difference (SMD) values of lipid profiles were computed to assess their association with pre-eclampsia at 95% CI. RESULTS: In this review a total of 15 observational studies were included. The mean values of triglyceride (TG), total cholesterol (TC), low density lipoprotein- cholesterol (LDL-c) and very low density lipoprotein- cholesterol (VLDL-c) were significantly higher in pre-eclamptic women as compared with normotensive pregnant women (TG = 229.61±88.27 and 147.00 ± 40.47, TC = 221.46 ± 45.90 and 189.67 ± 39.18, LDL = 133.92 ± 38.77 and 112.41 ± 36.08, VLDL = 41.44 ± 19.68 and 26.64 ± 7.87), respectively. The serum high density lipoprotein cholesterol (HDL-c) level was lower, but it is not statistically significant (HDL-c = 51.02 ± 16.01 and 61.80 ± 25.63) in pre-eclamptic women as compared with controls. The pooled standardized mean difference (SMD) of TG, TC, LDL-C and VLDL-C were significantly increased in pre-eclamptic women as compared with normotensive pregnant women with the SMD of (TG = 1.65 (1.10, 2.21), TC = 0.84 (0.40, 1.29), LDL-C = 0.95 (0.46, 1.45) and VLDL-C = 1.27 (0.72, 1.81)) at 95% CI, respectively, but the pooled SMD of HDL-cholesterol was decreased in pre-eclamptic women as compared with normotensive pregnant women (SMD = -0.91 (95% CI: -1.43, -0.39). CONCLUSIONS: In this review, the maternal serum levels of TG, TC, LDL-c and VLDL-c were significantly associated with the risk of preeclampsia. However, HDL- cholesterol was not significantly associated but it was lower in pre-eclamptic women. Further, large scale prospective studies should verify these outcomes and it is recommended that lipid profiles should be included as a routine diagnostic test for pre-eclamptic women.

[40] *Cybulska B, Kłosiewicz-Latoszek L, Penson PE et al.* **How much should LDL cholesterol be lowered in secondary prevention? Clinical efficacy and safety in the era of PCSK9 inhibitors**. Prog Cardiovasc Dis 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33383060

ABSTRACT

There is a strong evidence that more marked lowering of low-density lipoprotein cholesterol (LDL-C) leads to progressively lower risk of cardiovascular disease (CVD) events. The evidence on validity of

this hypothesis comes from epidemiological, genetic and clinical studies. The hypothesis "the lower the better" has been recently strongly supported by the results of secondary prevention trials with PCSK9 inhibitors. The combination of PCSK9 inhibitors and statins has resulted in achieving extremely low LDL-C levels with additional reduction of CVD events in secondary prevention. However, despite large clinical benefits, the safety of aggressive LDL-C lowering should be always taken into consideration, and there is still an ongoing discussion on whether very low LDL-C might result in some non-CVD adverse events. However, based on the available knowledge, so far the serious adverse events associated with achieving of very low LDL-C levels or intensive drug therapy have not been noted. These positive clinical effects were reflected in current ESC/EAS Guidelines (2019) for dyslipidaemia management. The experts strongly recommended the LDL-C lowering to levels that have been achieved in trials of PCSK9 inhibitors. In this state of the art review, we aimed to finally justify the critical need for LDL-C reduction to very low levels in secondary prevention patients in order to be as low as possible, as early as possible, and preferably lifelong.

[41] *Bruckert E, Desamericq G, Khachatryan A et al.* **Patient characteristics, treatment patterns, and adherence to lipid-lowering therapies following an acute coronary syndrome**. Reviews in cardiovascular medicine 2020; 21:643-650.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33388010
ABSTRACT
Despite dyslipidaemia management guidelines, many patients do not reach low-density lipoprotein cholesterol targets due to insufficiently intensive regimens or lack of adherence to their medication. This was a retrospective cohort study on the Pharmacoepidemiologic General Research eXtension (PGRx)-acute coronary syndrome (ACS) registry. Patients included were ≥ 18 years old who suffered an ACS between 2013 and 2016, and treated with lipid-lowering therapy (LLT) at hospital discharge or within 92 days. Patients were followed up to 12 months' post index ACS, a new cardiovascular event, loss to follow-up or death. Treatment intensity (high, moderate and low intensity statins ± ezetimibe) and adherence (proportion of days covered > 80%) are described. A total of 2,695 patients were included; mean age [SD] was 63.1 [12.8] years, and 77% were men. High, moderate and low intensity statins were started in 56% (1,520), 36% (971), and 3% (86) of patients, respectively. A further 2% (46) were on statin/ezetimibe combination, 2% (42) on other LLT and 1% (30) on ezetimibe alone. At follow-up, around 70% of patients were adherent to LLT, with those on moderate intensity treatments showing better adherence (76%) than those on low (63%) or high (67%) intensity treatments. Despite guideline recommendations, many patients following an ACS are not treated with high intensity statins, and adherence remains far from optimal. Effort should be made to increase the proportion of patients treated with high intensity statins following an ACS and to further improve treatment adherence.

[42] *Ruffatti A, Tonello M, Favaro M et al.* **The efficacy and safety of second-line treatments of refractory and/or high risk pregnant antiphospholipid syndrome patients. A systematic literature review analyzing 313 pregnancies**. Seminars in arthritis and rheumatism 2020; 51:28-35.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33360227
ABSTRACT
OBJECTIVE: The most efficacious strategy to manage pregnant patients with antiphospholipid syndrome (APS) refractory to conventional heparin/low-dose aspirin treatment or at high risk of

adverse pregnancy outcomes has not been determined with any degree of certainty. The study set out to evaluate the efficacy and safety of the second-line treatments most frequently used in addition to conventional therapy, and the data were analyzed to identify which is/are associated to the best pregnancy outcomes. METHODS: A systematic review of the literature on studies concerning second-line treatments for refractory and/or high risk pregnant APS women published between February 2006 and February 2020 was conducted. The records were retrieved by searching Medline via Pubmed, the Web of Science platform, the Cochrane library database and clinicaltrials.gov. RESULTS: Fourteen studies met the eligibility criteria of the review: six retrospective cohort studies, one case-control, one case-series and six case reports. The results of single treatment protocols based upon hydroxychloroquine (HCQ), low-dose steroids (LDS), intravenous immunoglobulins (IVIG), plasma exchange (PE) or pravastatin and of combination protocols based upon HCQ+LDS, IVIG+LDS, PE+LDS and PE+IVIG used during 313 pregnancies in 303 APS women were analyzed and compared. The second-line treatments produced 261/313 (83.4%) live births; severe pregnancy complications were registered in 75/313 (24%) pregnancies. Drug side-effects were observed in 3/313 (0.9%) pregnancies. Statistical analysis identified a significantly higher live birth rate and/or a significantly lower number of severe complications in the pregnancies treated with IVIG, HCQ, pravastatin, PE+IVIG and PE+LDS. CONCLUSION: Our results suggest using low-dose IVIG (< 2 g/Kg/month) or HCQ 400 mg/day starting before pregnancy in women with APS refractory to conventional therapy, while high-dose IVIG (2 g/Kg/month) associated with PE or alone in those with high risk±refractory APS.

[43] *Urbánek R, Tichý L, Freiberger T*. **Tangier disease in family with the phenotype of familial hypercholesterolemia**. Vnitr Lek 2020; 66:443-446.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33380124
ABSTRACT
Within the project MedPed (Make Early Diagnosis to Prevent Deaths) we have examined patient with familial hypercholesterolemia in our lipid ambulance. During the following investigation of the patients family we found out that her sister has on the contrary very low levels of total and LDL-cholesterol. Concentration of HDL-cholesterol was extreamly low (almost immeasurable). Differential diagnosis uttered a suspicion of rare form of familial hypoalfalipoproteinemia so-called Tangier disease. This suspicion was then confirmed by molecular genetic examination. Tangier disease is a rare lipoprotein metabolism disorder characterized biochemically by almost complete absence of plasmatic HDL-cholesterol, extremely low level of apolipoprotein A-I and accumulation of cholesterol esters in macrophages. The first case was recorded on the Tangier island in 1961. In our research we describe the first case of a patient with homozygous form of Tangier disease in the history of the Czech Republic.

[44] *Liu ZL, Ou ZJ, Ou JS*. **[Association between protein modification of high density lipoprotein and cardiovascular diseases]**. Zhonghua xin xue guan bing za zhi 2020; 48:1078-1082.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33355754
ABSTRACT

[45] *Wang Y, Wang QY, Guan C et al.* **[Association between lipoprotein (a) level and chronic cardio-renal syndrome in elderly patients]**. Zhonghua xin xue guan bing za zhi 2020; 48:1047-1052.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33355749
ABSTRACT
Objective: To explore the relationship between lipoprotein(a) [Lp(a)] and chronic cardio-renal syndrome (CRS) in elderly patients. Methods: Chronic heart failure (CHF) patients age ≥ 65 years old, who hospitalized in the department of Cardiology of Hebei General Hospital from December 2017 to October 2019, were included in this study. According to the estimate glomerular filtration rate (eGFR) level, patients were divided into CRS group (eGFR<60 ml·min(-1)·1.73 m(-2)) and CHF group (eGFR ≥60 ml·min(-1)·1.73 m(-2)). The blood index and basic disease information were collected and compared. Left ventricular ejection fraction (LVEF) were measured by echocardiography. The correlation between clinical indicators and cardio-renal function (LVEF and eGFR) was assessed. The multivariate logistic regression analysis was used to evaluate the related risk factors of CRS in elderly patients; subgroup logistic regression analysis was performed according to the basic disease of patients to assess the relationship between Lp(a) and CRS. Results: A total of 172 elderly patients (85 males (49.4%), aged 79 (71, 84) years) were finally enrolled. Among them, 88 cases (51.2%) were in CRS group and 84 cases (48.8%) were in CHF group. Age (80 (74, 84) years old vs. 74 (70, 82) years old) and LP (a) levels (222.0 (112.0, 445.3) mg/L vs. 155.0 (97.0, 348.7) mg/L) were significantly higher in the CRS group than in the CHF group (P<0.05). Lp(a) levels were negatively correlated with LVEF (r=-0.155, P=0.043) and eGFR (r=-0.220, P=0.004) in total cohort. In the subgroup analysis of patients with 2 high-incidence basic diseases (coronary heart disease and hypertension), Lp(a) was negatively correlated with LVEF (r=-0.250, P=0.007) in the coronary heart disease group, and negatively correlated with eGFR (r=-0.233, P=0.013) in the hypertension group. Multivariate logistic regression analysis showed that age (OR = 1.069, 95%CI: 1.017-1.124, P= 0.009) and Lp(a) (OR = 3.719, 95%CI: 1.339-10.326, P = 0.012) were independent correlates of CRS. The results of logistic regression analysis showed that Lp(a) was an independent correlative factor of CRS in the subgroups of coronary heart disease (OR=3.207, 95%CI: 1.129-9.108, P=0.029) and hypertension (OR=3.054, 95%CI: 1.086-8.587, P=0.034). Conclusion: Serum Lp(a) level is independently related with CRS in elderly patients.

[46] *Ye P*. **[Highlight the importance of reaching the target goal of LDL-C in extremely-high-risk ASCVD patients: follow the trend of combined use of lipid lowering medications]**. Zhonghua xin xue guan bing za zhi 2020; 48:998-999.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33355746
ABSTRACT

[47] *Zeng YY, Liu J, Liu J et al.* **[The expanding needs on lipid-lowering treatment in patients with acute coronary syndrome by applying newly issued definition of extreme high-risk by Chinese Society of Cardiology]**. Zhonghua xin xue guan bing za zhi 2020; 48:1039-1046.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33355748
ABSTRACT
Objective: To assess the expanding needs on lipid-lowering treatment in patients with acute coronary syndrome (ACS) by applying newly issued definition of extreme high-risk, which is proposed by

Literature update week 53 (2020)

Chinese expert consensus on lipid management of extreme high-risk atherosclerotic cardiovascular disease (ASCVD) patients of Chinese Society of Cardiology (CSC). Methods: Data of this study was derived from the Improving Care for Cardiovascular Disease in China (CCC) project, which was a case-based nationwide registry study and launched as a collaborative initiative by the American Heart Association and the CSC. The project consecutively recruited ACS patients from158 tertiary hospitals and 82 second hospitals across China, and detailed clinical information of patients was collected. This study enrolled ACS inpatients in CCC project from November 2014 to July 2019. The proportion of extreme high-risk patients, their characteristics, mean LDL-C levels at admission, the gap between measured LDL-C level and the new target, and lipid-lowering therapy at discharge were assessed. Results: Among 104 516 ACS inpatients enrolled in this study, 75.1% (78 527/104 516) met the criteria of extreme high-risk and were expected to achieve the new LDL-C goal. Among patients at extreme high-risk, 21.2% (16 651/78 527) had multiple severe ASCVD events and 78.8% (61 876/78 527) had 1 severe ASCVD event and at least two high-risk factors. For the extreme high-risk patients, the mean level of LDL-C at admission was (2.8±1.0) mmol/L, prevalence of LDL-C ≥1.4 mmol/L was 93.4% (73 307/78 527) and the median gap between LDL-C level at admission and the target of 1.4 mmol/L was 1.3 (0.8, 2.0) mmol/L. If LDL-C could be further reduced to 50% of the admission level, we estimated that 55.6% (43 632/78 527) of the extreme high-risk patients would achieve the new LDL-C goal. Among 40 875 patients with information about discharge statin dosage, 93.5% (28 004/29 947) of the extreme high-risk patients were prescribed with statins at discharge, and among them 95.1% (26 632/28 004) received statin monotherapy and 91.1% (25 501/28 004) were at moderate doses of statins. Conclusion: About three fourth of inpatients with ACS were categorized as extreme high-risk based on the new definition of CSC expert consensuses, nine out of ten patients at extreme high-risk didn't achieve the new LDL-C target at admission, and the intensity of lipid-lowering therapy was insufficient in clinical practice. There are substantially expanding needs for implementing more intensive and effective lipid-lowering strategies.