[1] *Tombling BJ, Zhang Y, Huang YH et al.* **The emerging landscape of peptide-based inhibitors of PCSK9**. Atherosclerosis 2021; 330:52-60.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34246818

ABSTRACT

Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a clinically validated target for treating cardiovascular disease (CVD) due to its involvement in cholesterol metabolism. Although approved monoclonal antibodies (alirocumab and evolocumab) that inhibit PCSK9 function are very effective in lowering cholesterol, their limitations, including high treatment costs, have so far prohibited widespread use. Accordingly, there is great interest in alternative drug modalities to antibodies. Like antibodies, peptides are valuable therapeutics due to their high target potency and specificity. Furthermore, being smaller than antibodies means they have access to more drug administration options, are less likely to induce adverse immunogenic responses, and are better suited to affordable production. This review surveys the current peptide-based landscape aimed towards PCSK9 inhibition, covering pre-clinical to patented drug candidates and comparing them to current cholesterol lowering therapeutics. Classes of peptides reported to be inhibitors include nature-inspired disulfide-rich peptides, combinatorially derived cyclic peptides, and peptidomimetics. Their functional activities have been validated in biophysical and cellular assays, and in some cases pre-clinical mouse models. Recent efforts report peptides with potent sub-nanomolar binding affinities to PCSK9, which highlights their potential to achieve antibody-like potency. Studies are beginning to address pharmacokinetic properties of PCSK9-targeting peptides in more detail. We conclude by highlighting opportunities to investigate their biological effects in pre-clinical models of cardiovascular disease. The anticipation concerning the PCSK9-targeting peptide landscape is accelerating and it seems likely that a peptide-based therapeutic for treating PCSK9-mediated hypercholesterolemia may be clinically available in the near future.

[2] *Sciarrillo CM, Koemel NA, Keirns BH et al.* **Who would benefit most from postprandial lipid screening?** Clinical nutrition (Edinburgh, Scotland) 2021; 40:4762-4771.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34242916

ABSTRACT

BACKGROUND & AIMS: Individuals with fasting triglycerides (TG) <150 mg/dL can experience a deleterious postprandial TG response ≥220 mg/dL to a high-fat meal (HFM). The purpose of this study was to identify individuals based on fasting TG that would benefit most from additional postprandial screening. METHODS: We conducted a secondary analysis of 7 studies from our laboratories featuring 156 disease-free participants (64 M, 92 F; age 18-70 years; BMI 18.5-30 kg/m(2)). Participants observed a 10-12 h overnight fast, after which they consumed an HFM (10-13 kcal/kg body mass; 61-64% kcal from fat). Two methods were used to identify lower and upper fasting TG cut points. Method 1 identified the lower limit as the TG concentration at which ≥90% of individuals presented peak postprandial TG (PPTG) <220 mg/dL and the upper limit as the concentration which ≥90% of individuals presented PPTG ≥220 mg/dL. Method 2 utilized receiver operating characteristic (ROC) curves and identified the lower limit as the fasting TG concentration where sensitivity was ≈95% and the upper limit as the concentration at which specificity was ≈95%. RESULTS: In Method 1, 90% of individuals with fasting TG >130 mg/dL (>1.50 mmol/L) exhibited PPTG ≥220 mg/dL (≥2.50 mmol/L), while 100% of individuals with fasting TG <66 mg/dL (0.75 mmol/L) had PPTG that did not exceed 220 mg/dL (2.50 mmol/L). In Method 2, when sensitivity

was ≈95%, the corresponding fasting TG concentration was 70 mg/dL (0.79 mmol/L). When specificity was ≈95%, the corresponding fasting TG concentration was 114 mg/dL (1.29 mmol/L). Based on methods 1 and 2, there was a moderate positive association ($r = 0.37$, $p < 0.004$) between fasting and PPTG for individuals with fasting TG between 70 and 130 mg/dL (0.79-1.50 mmol/L), in which 24% exhibited PPTG ≥220 mg/dL (≥2.50 mmol/L) while 76% did not. CONCLUSIONS: Postprandial TG testing is likely most useful for individuals with fasting TG concentrations between 70 and 130 mg/dL (0.79-1.50 mmol/L). Outside of this range, postprandial TG responses are largely predictable. Establishing a specific patient group for which postprandial TG testing is most useful may lead to earlier risk detection in these individuals.

[3] *Rhainds D, Brodeur MR, Tardif JC*. **Lipoprotein (a): When to Measure and How to Treat?** Current atherosclerosis reports 2021; 23:51.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34235598
ABSTRACT
PURPOSE OF REVIEW: The purpose of this article is to review current evidence for lipoprotein (a) (Lp(a)) as a risk factor for multiple cardiovascular (CV) disease phenotypes, provide a rationale for Lp(a) lowering to reduce CV risk, identify therapies that lower Lp(a) levels that are available clinically and under investigation, and discuss future directions. RECENT FINDINGS: Mendelian randomization and epidemiological studies have shown that elevated Lp(a) is an independent and causal risk factor for atherosclerosis and major CV events. Lp(a) is also associated with non-atherosclerotic endpoints such as venous thromboembolism and calcific aortic valve disease. It contributes to residual CV risk in patients receiving standard-of-care LDL-lowering therapy. Plasma Lp(a) levels present a skewed distribution towards higher values and vary widely between individuals and according to ethnic background due to genetic variants in the LPA gene, but remain relatively constant throughout a person's life. Thus, elevated Lp(a) (≥50 mg/dL) is a prevalent condition affecting >20% of the population but is still underdiagnosed. Treatment guidelines have begun to advocate measurement of Lp(a) to identify patients with very high levels that have a family history of premature CVD or elevated Lp(a). Lipoprotein apheresis (LA) efficiently lowers Lp(a) and was recently associated with a reduction of incident CV events. Statins have neutral or detrimental effects on Lp(a), while PCSK9 inhibitors significantly reduce its level by up to 30%. Specific lowering of Lp(a) with antisense oligonucleotides (ASO) shows good safety and strong efficacy with up to 90% reductions. The ongoing CV outcomes study Lp(a)HORIZON will provide a first answer as to whether selective Lp(a) lowering with ASO reduces the risk of major CV events. Given the recently established association between Lp(a) level and CV risk, guidelines now recommend Lp(a) measurement in specific clinical conditions. Accordingly, Lp(a) is a current target for drug development to reduce CV risk in patients with elevated levels, and lowering Lp(a) with ASO represents a promising avenue.

[4] *Parkkila K, Kiviniemi A, Tulppo M et al.* **Abdominal aorta plaques are better in predicting future cardiovascular events compared to carotid intima-media thickness: A 20-year prospective study**. Atherosclerosis 2021; 330:36-42.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34229196
ABSTRACT

BACKGROUND AND AIMS: Both carotid intima-media thickness (IMT) and arterial plaques have been shown to predict future CV events. Since there are no previous studies on the subject, our objective was to compare carotid IMT and the length of plaques in abdominal-pelvic main arteries in CV risk assessment in a prospective study setting with a follow-up of over 20 years. METHODS: A total of 1007 patients (50% men), aged 51 ± 6.0 years, participated in the current study. Carotid IMT and the summarized plaque length (SUM) from abdominal aorta to common femoral arteries were ultrasonographically assessed. Patients were followed-up a median (1st-3rd quartile) of 22.5 (17.5-23.2) years for CV events. RESULTS: SUM significantly predicted CV events (HR per every 10 mm increase: 1.035, 95% CI: 1.027-1.044, $p < 0.001$). Those in the highest SUM tertile had over 3-fold risk for CV event (HR: 3.392, 95% CI: 2.427-4.741, $p < 0.001$) when compared to those in the lowest tertile. SUM significantly predicted CV events even after adjusting for age, sex, hypertension, diabetes, smoking (pack-years), LDL cholesterol and IMT. Adding SUM to the established model improved C-index (95% CI) from 0.706 (0.674-0.738) to 0.718 (0.688-0.747) as well as both discrimination ($p < 0.001$) and reclassification ($p < 0.001$) of the patients. In contrast, IMT predicted cardiovascular events only in univariate analysis and it did not improve discrimination or reclassification of the patients. CONCLUSIONS: In light of our findings, SUM is a superior indicator and clinical tool for evaluating the overall CV risk compared to carotid IMT.

[5] *Oliver PJ, Arutla S, Yenigalla A et al.* **Lipid Nutrition in Asthma**. Cell biochemistry and biophysics 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34244966

ABSTRACT

Asthma is a heterogeneous pulmonary disease that has constantly increased in prevalence over the past several decades. Primary symptoms include airway constriction, airway hyperresponsiveness, and airway remodeling with additional symptoms such as shortness of breath, wheezing, and difficulty breathing. Allergic asthma involves chronic inflammation of the lungs, and the rise in its yearly diagnosis is potentially associated with the increased global consumption of foods similar to the western diet. Thus, there is growing interest into the link between diet and asthma symptoms, with mounting evidence for an important modulatory role for dietary lipids. Lipids can act as biological mediators in both a proinflammatory and proresolution capacity. Fatty acids play key roles in signaling and in the production of mediators in the allergic and inflammatory pathways. The western diet leads to a disproportionate ω-6:ω-3 ratio, with drastically increased ω-6 levels. To counteract this, consumption of fish and fish oil and the use of dietary oils with anti-inflammatory properties such as olive and sesame oil can increase ω-3 and decrease ω-6 levels. Increasing vitamin intake, lowering LDL cholesterol levels, and limiting consumption of oxidized lipids can help reduce the risk of asthma and the exacerbation of asthmatic symptoms. These dietary changes can be achieved by increasing intake of fruits, vegetables, nuts, oily fish, seeds, animal-related foods (eggs, liver), cheeses, grains, oats, and seeds, and decreasing consumption of fried foods (especially fried in reused oils), fast foods, and heavily processed foods.

[6] *Oh PC, Jang AY, Ha K et al.* **Effect of Atorvastatin (10 mg) and Ezetimibe (10 mg) Combination Compared to Atorvastatin (40 mg) Alone on Coronary Atherosclerosis**. The American journal of cardiology 2021; 154:22-28.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34238445

ABSTRACT
It remains inconclusive whether the additional low-density lipoprotein cholesterol (LDL-C) lowering effects of ezetimibe added to statin on coronary atherosclerosis and clinical outcomes are similar to those of statin monotherapy in the setting of comparable LDL-C reduction. We aimed to determine whether there were distinguishable differences in their effects on coronary atherosclerosis with intermediate stenosis between the combination of moderate-intensity statin plus ezetimibe and high-intensity statin monotherapy. Forty-one patients with stable angina undergoing percutaneous coronary intervention were randomized to receive either atorvastatin 10 mg plus ezetimibe 10 mg (ATO10/EZE10) or atorvastatin 40 mg alone (ATO40). The intermediate lesions were evaluated using a near-infrared spectroscopy-intravascular ultrasonography at baseline and after 12 months in 37 patients. The primary endpoint was percent atheroma volume (PAV). Mean LDL-C levels were significantly reduced by 40% and 38% from baseline in the ATO10/EZE10 group (n = 18, from 107 mg/dL to 61 mg/dL) and ATO40 group (n = 19, from 101 mg/dL to 58 mg/dL), respectively, without between-group difference. The absolute change of PAV was -2.9% in the ATO10/EZE10 group and -3.2% in the ATO40 group. The mean difference (95% confidence interval) for the absolute change in PAV between the 2 groups was 0.5% (-2.4% to 2.8%), which did not exceed the pre-defined non-inferiority margin of 5%. There was no significant reduction in lipid core burden index in both groups. In conclusion, the combination of atorvastatin 10 mg and ezetimibe 10 mg showed comparable LDL-C lowering and regression of coronary atherosclerosis in the intermediate lesions, compared with atorvastatin 40 mg alone.

[7] Narayanaswamy M, Sharma S. Polygenic Hypercholesterolemia. In: StatPearls. Treasure Island (FL): StatPearls Publishing
Copyright © 2021, StatPearls Publishing LLC.; 2021.
[8] *Lohia P, Kapur S, Benjaram S et al.* **Statins and clinical outcomes in hospitalized COVID-19 patients with and without Diabetes Mellitus: a retrospective cohort study with propensity score matching**. Cardiovascular diabetology 2021; 20:140.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34246277
ABSTRACT
BACKGROUND: The pleiotropic effects of statins may reduce the severity of COVID-19 disease. This study aims to determine the association between inpatient statin use and severe disease outcomes among hospitalized COVID-19 patients, especially those with Diabetes Mellitus (DM). RESEARCH DESIGN AND METHODS: A retrospective cohort study on hospitalized patients with confirmed COVID-19 diagnosis. The primary outcome was mortality during hospitalization. Patients were classified into statin and non-statin groups based on the administration of statins during hospitalization. Analysis included multivariable regression analysis adjusting for confounders and propensity score matching to achieve a 1:1 balanced cohort. Subgroup analyses based on presence of DM were conducted. RESULTS: In the cohort of 922 patients, 413 had a history of DM. About 27.1% patients (n = 250) in the total cohort (TC) and 32.9% patients (n = 136) in DM cohort received inpatient statins. Atorvastatin (n = 205, 82%) was the most commonly prescribed statin medication in TC. On multivariable analysis in TC, inpatient statin group had reduced mortality compared to the non-statin group (OR, 0.61; 95% CI, 0.42-0.90; p = 0.01). DM modified this association between inpatient statins and mortality. Patients with DM who received inpatient statins had reduced mortality (OR, 0.35; 95% CI, 0.21-0.61; p < 0.001). However, no such association was noted among patients

without DM (OR, 1.21; 95% CI, 0.67-2.17; p=0.52). These results were further validated using propensity score matching. CONCLUSIONS: Inpatient statin use was associated with significant reduction in mortality among COVID-19 patients especially those with DM. These findings support the pursuit of randomized clinical trials and inpatient statin use appears safe among COVID-19 patients.

[9] *Liu HH, Li S, Cao YX et al.* **Association of triglyceride-rich lipoprotein-cholesterol with recurrent cardiovascular events in statin-treated patients according to different inflammatory status**. Atherosclerosis 2021; 330:29-35.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34225103
ABSTRACT
BACKGROUND AND AIMS: The association of triglyceride-rich lipoprotein-cholesterol (TRL-C) with recurrent cardiovascular events (RCVEs) has not been studied. Moreover, whether inflammation can affect TRL-C-associated cardiovascular risk is unknown. This study sought to examine the association between TRL-C and RCVEs, and whether this relationship is modulated by systemic inflammation in statin-treated patients with coronary artery disease (CAD) and nearly normal triglyceride. METHODS: In this study, 6723 CAD patients were consecutively enrolled, following a first CVE with triglyceride <2.3 mmol/L. Baseline lipid profile and high-sensitivity C-reactive protein (hsCRP) levels were determined. All patients were searched for RCVEs. The risk of RCVEs was assessed across quartiles (Q) of baseline TRL-C and further stratified by the median of hsCRP. RESULTS: Over a mean follow-up of 58.91 ± 17.79 months, 538 RCVEs were recorded. After adjustment for potential confounders, Q4 of TRL-C was significantly associated with the risk of RCVEs, which remained unchanged after hsCRP stratification. When subjects were grouped according to both TRL-C and hsCRP levels, patients with Q4 of TRL-C and hsCRP had the highest increase of the risk of RCVEs compared with the reference group (TRL-C Q1-3 and hsCRP Q1-3; HR, 1.90; 95%CI: 1.27-2.87). Furthermore, adding TRL-C to the original predicting model led to a slight but significant improvement. CONCLUSIONS: The present analysis firstly showed that elevated TRL-C was associated with an increased RCVEs risk in statin-treated patients with CAD independent of systemic inflammation, suggesting that it might be a useful marker for risk stratification and a treatment target in this patient population.

[10] *Kobayashi J, Minamizuka T, Koshizaka M et al.* **Serum HDL-C values: An extremely useful marker for differentiating homozygous lipoprotein lipase deficiency from severe hypertriglyceridemia with other causes in Japan: A meta-analysis based on literatures on Japanese homozygous lipoprotein lipase deficiency**. Clinica chimica acta; international journal of clinical chemistry 2021; 521:85-89.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34242636
ABSTRACT
BACKGROUNDS AND AIM: Lipoprotein lipase (LPL) deficiency is a genetic disorder with a defective gene for lipoprotein lipase, leading to very high triglycerides. In the daily practice it is much more common to come across severely hypertriglyceridemia without homozygous or compound heterozygous LPL deficiency (SHTG). METHODS: We investigated on how to screen homozygous or compound heterozygous LPL deficiency using lipid parameters by meta-analyzing past 20 subjects on this genetic disease reported by Japanese investigators. As a comparison with LPL deficiency, 21 subjects with SHTG from recent two studies were included in this study. RESULTS: Serum HDL-C

levels were significantly lower in LPL deficiency than in SHTG (0.38 ± 0.13 vs 0.94 ± 0.28 mmol/L (mean ± SD), $p < 0.001$), whereas other serum lipids did not differ between the two groups. The ROC curve ± standard error for serum HDL-C for discriminating the two groups was 0.97 ± 0.019. Sensitivity and specificity for distinguishing the two groups were 90% and 95%, respectively when serum HDL-C 0.62 mmol/L was adopted as cut point. CONCLUSION: We found for the first time that serum HDL-C is an extremely useful marker for discriminating LPL deficiency from SHTG in Japanese population.

[11] *Jia J, Zhang L, Wang L et al.* **A systematic review and meta-analysis on the efficacy of statins in the treatment of atherosclerosis**. Ann Palliat Med 2021; 10:6793-6803.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34237978

ABSTRACT

BACKGROUND: It was a meta-analysis on the efficacy of statins in the treatment of atherosclerosis. METHODS: The PubMed, Medline, Embase, Web of Sciences, and other Chinese and English databases were used to retrieve literature on randomized controlled trials (RCTs) of statins in the treatment of atherosclerosis, published from January 2000 to January 2021. The Cochrane Handbook for Systematic Reviews of Intervention 5.0.2 was used to conduct bias risk assessment, and Review Manager 5.3 software (RevMan) was used for meta-analysis. RESULTS: A total of 12 articles with 1,180 participants were included in the meta-analysis. In the observation group, the plaque area [mean difference (MD) =-1.21; 95% confidence interval (CI): -2.03 to -0.38; Z =2.87; P=0.004], total cholesterol (TC) level (MD =-0.72; 95% CI: -1.01 to -0.43; Z =4.83; P<0.00001), triglyceride (TG) level (MD =-0.43; 95% CI: -0.76 to -0.09; Z =2.51; P=0.01), and the low-density lipoprotein (LDL-C) level (MD =-0.79; 95% CI: -1.41 to -0.18; Z =2.54; P=0.01) were lower, while the clinical effective rate (MD =3.64; 95% CI: 1.39 to 9.53; Z =2.64; P=0.008) was higher, and the difference was notable. No notable difference was noted in intra-media thickness (IMT) (MD =-0.41; 95% CI: -0.88 to -0.06; Z =1.7; P=0.09), hypersensitive C-reactive protein (hs-CRP) level (MD =-1.61; 95% CI: -3.59 to 0.37; Z =1.7; P=0.09), and high-density lipoprotein (HDL-C) level (MD =0.14; 95% CI: -0.02 to 0.30; Z =2.54; P=0.09) between the 2 groups. DISCUSSION: The use of statins in the treatment of atherosclerosis can reduce the levels of TC, TG, and LDL-C, mitigate clinical symptoms, and reduce blood lipids with good efficacy.

[12] *Jain V, Al Rifai M, Mahtta D et al.* **Highlights from Studies Presented at the Virtual American College of Cardiology Scientific Sessions 2021: Staying Updated with the Latest Advancements in Prevention**. Current atherosclerosis reports 2021; 23:50.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34226979

ABSTRACT

PURPOSE OF REVIEW: This review highlights late-breaking science presented at the Virtual American College of Cardiology Scientific Sessions 2021 that demonstrated advancements in preventative cardiology and introduced novel therapeutic modalities for the management of chronic kidney disease, heart failure, and COVID-19. RECENT FINDINGS: The studies reviewed include clinical trials that assessed the use of dapagliflozin in patients with respiratory failure due to COVID-19 (DARE-19 trial); evinacumab for patients with severe hypertriglyceridemia and pancreatitis; effect of genotype-guided oral P2y12 inhibitors vs conventional clopidogrel on long-term ischemic outcomes after percutaneous coronary intervention (TAILOR-PCI trial); anticoagulation in patients hospitalized

with COVID-19 (ACTION trial); atorvastatin vs placebo in patients with COVID-19 admitted to the ICU (INSPIRATION-S trial); rehabilitation therapy in older acute heart failure patients (REHAB-HF trial); and aspirin dosing: a patient-centric trial assessing benefits and long-term effectiveness (ADAPTABLE trial). In addition, we review the results of the American College of Cardiology Global Heart Attack Initiative (GHATI). Finally, we discuss the secondary analysis of the STRENGTH trial assessing the association of achieved levels of omega-3 fatty acid levels and major cardiovascular outcomes. The studies presented at the virtual American College of Cardiology Scientific Session 2021 represent remarkable contributions in the field of cardiovascular disease and prevention.

[13] *Franchi C, Lancellotti G, Bertolotti M et al.* **Use of Lipid-Lowering Drugs and Associated Outcomes According to Health State Profiles in Hospitalized Older Patients**. Clin Interv Aging 2021; 16:1251-1264.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34239298

ABSTRACT

OBJECTIVE: To assess how lipid-lowering drugs (LLDs) are administered in the hospitalized patients aged 65 and older and their association with clinical outcomes according to their health-related profiles. DESIGN: This is a retrospective study based on data from REPOSI (REgistro POliterapie SIMI - Italian Society of Internal Medicine) register, an Italian network of internal medicine hospital wards. SETTING AND PARTICIPANTS: A total of 4642 patients with a mean age of 79 years enrolled between 2010 and 2018. METHODS: Socio-demographic characteristics, functional abilities, cognitive skills, laboratory parameters and comorbidities were used to investigate the health state profiles by using multiple correspondence analysis and clustering. Logistic regression was used to assess whether LLD prescription was associated with patients' health state profiles and with short-term mortality. RESULTS: Four clusters of patients were identified according to their health state: two of them (Cluster III and IV) were the epitome of frailty conditions with poor short-term outcomes, whereas the others included healthier patients. The average prevalence of LLD use was 27.6%. The lowest prevalence was found among the healthier patients in Cluster I and among the oldest frail patients with severe functional and cognitive impairment in Cluster IV. The highest prevalence was among multimorbid patients in Cluster III (OR=4.50, 95% CI=3.76-5.38) characterized by a high cardiovascular risk. Being prescribed with LLDs was associated with a lower 3-month mortality, even after adjusting for cluster assignment (OR=0.59; 95% CI = 0.44-0.80). CONCLUSION: The prevalence of LLD prescription was low and in overall agreement with guideline recommendations and with respect to patients' health state profiles.

[14] *Du X, Xin H.* **Association between cholesterol intake and all-cause mortality: NHANES-linked mortality study**. Cent Eur J Public Health 2021; 29:117-121.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34245551

ABSTRACT

OBJECTIVES: There has been insufficient evidence for a quantitative recommendation for dietary cholesterol, therefore, we aim to investigate the optimal cholesterol intake related to a lower all-cause mortality risk. METHODS: The National Health and Nutrition Examination Survey (NHANES) is a large population survey to investigate public health in the United States. We analysed data from 1999-2002 linked with mortality data obtained through 2006. Cox proportional hazard ratios (HRs) with 95% confidence intervals (CIs) were estimated to assess risks for all-cause mortality associated

with cholesterol intake. RESULTS: A total of 7,728 participants were analysed in the present study, and 519 assumed death events. Compared with the third quartile (216-373 mg/day) of cholesterol intake, the risks of mortality increased in both the first two and the last quartiles (quartile 1: HR 1.53, 95% CI 1.16-2.00; quartile 2: HR 1.22, 95% CI 0.94-1.60; quartile 4: HR 1.39, 95% CI 1.05-1.83). The association between cholesterol intake and the risk of all-cause mortality followed a U-shaped curve, with the cholesterol intake associated with the lowest mortality being 328 mg/day. CONCLUSIONS: The present study suggests an optimal cholesterol intake for lowering the all-cause mortality risk.

[15] *Bao J, Zheng S, Huang J et al.* **Mental health is correlated with lipoprotein(a) levels in male patients with premature coronary heart disease**. Ann Palliat Med 2021; 10:6482-6492.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34237965
ABSTRACT
BACKGROUND: High levels of lipoprotein(a) (Lp(a)) is an independent risk factor for premature coronary heart disease (PCHD). It is also considered a residual risk for controlled low density lipoprotein cholesterol (LDL-C). Dietary control, exercise, and drugs have limited effects on the levels of Lp(a). Recently, mental health was found to be associated with lipid levels and increased risk of PCHD. However, the relationship between mental health and Lp(a) is still unknown. This study explored the association between mental health and Lp(a) levels in men with PCHD. METHODS: A retrospective, observational study was conducted. A total of 226 male patients with PCHD, aged 49.65±3.68 years, was included in this study. The control group consisted of 230 age-matched healthy male volunteers. Serum Lp(a) levels ≥30 mg/dL, as measured by the immunoturbidimetry method, were considered high. All participants received health related quality of life (HRQoL) scores using the self-assessed 36-Item Short Form Health Survey (SF-36). The HRQoL includes both a physical component summary (PCS) and a mental component summary (MCS). RESULTS: Patients with PCHD were found to have higher levels of Lp(a) (51.61±33.39 vs. 26.42±21.93, P<0.001), and lower MCS (35.83±4.21 vs. 39.85±4.12) and PCS scores (38.02±3.73 vs. 39.63±3.21) compared to healthy volunteers. The MCS score was negatively correlated with Lp(a) levels in the PCHD group (R=-0.295, P<0.001), but no correlation was detected in the control group. There was no relationship between the PCS score and Lp(a) levels in neither the PCHD group nor the healthy control group. Multivariate logistic regression analysis indicated that the MCS and PCS scores were negatively correlated with the risk of PCHD. CONCLUSIONS: These findings suggested that poor mental health may be associated with high levels of Lp(a) and increased risk of PCHD in men. Therefore, improving the mental state in men with PCHD may be crucial.

[16] *Zippl AL, Seeber B, Wildt L*. **Obesity and infertility: Are hyperlipidemia and hyperinsulinemia the bad guys?** Fertil Steril 2021; 116:365-366.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34233840
ABSTRACT

[17] *Vlad CE, Foia L, Pavel-Tanasa M et al.* **Evaluation of cardiovascular events and progression to end-stage renal disease in patients with dyslipidemia and chronic kidney disease from the North-Eastern area of Romania**. International urology and nephrology 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34224064
ABSTRACT

PURPOSE: The aim of this prospective cohort study was: to identify the association between different biomarkers [proprotein convertase subtilisin/kexin 9-PCSK9, lipoprotein(a)-Lp(a) and high-sensitivity C-reactive protein-hsCRP] and the cardiovascular events; to evaluate the relationship between the 3 biomarkers mentioned above and the renal outcomes that contributed to end-stage renal disease (ESRD). METHODS: We studied 110 patients with chronic kidney disease (CKD) stages 2 to 4. The identification of the new cardiovascular events and the renal outcomes were performed by clinical and paraclinical explorations. RESULTS: 350 patients were examined and 110 (31.4%) were included in this study. The mean age was 55.6±10.9 years, with a higher number of men compared to women. The CKD patients with de novo cardiovascular events and new renal outcome during the study, had significantly increased values of total cholesterol (TC), low density cholesterol lipoprotein (LDL-C) at 6 and 12 months and higher levels of Lp(a), PCSK9, hsCRP and low ankle-brachial index (ABI) and ejection fraction (EF) values compared to patients without cardiovascular and renal events. In CKD patients, PCSK9>220 ng/mL was a predictor of cardiovascular events, while the EF<50% was a predictor for renal outcomes. For CKD patients with PCSK9>220 ng/mL and hsCRP>3 mg/L levels, the time-interval for the new cardiovascular and renal events occurrence were significantly decreased compared to patients displaying low values of these biomarkers. CONCLUSION: The results of this study show that PCSK9>220 ng/mL was predictor for cardiovascular events, while EF<50% was predictor for CKD progression to ESRD. PCSK9>220 ng/mL and hsCRP>3 mg/L were associated with the occurrence of renal and cardiovascular events earlier.

[18] *Rollefstad S, Ikdahl E, Wibetoe G et al.* **An international audit of the management of dyslipidaemia and hypertension in patients with rheumatoid arthritis-results from 19 countries**. European heart journal. Cardiovascular pharmacotherapy 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34232315

ABSTRACT

AIMS: To assess differences in estimated cardiovascular disease (CVD) risk among rheumatoid arthritis (RA) patients from different world regions. Further to evaluate the management and goal attainment of lipids and blood pressure (BP). METHODS AND RESULTS: The SUrvey of CVD Risk Factors in patients with RA was conducted in 14503 patients from 19 countries during 2014-2019. The treatment goal for BP was <140/90 mmHg. CVD risk prediction and lipid goals were according to the 2016 European guidelines. Overall, 21% had a very high estimated risk of CVD, ranging from 5% in Mexico, 15% in Asia, 19% in Northern Europe, to 31% in Central and Eastern Europe and 30% in North America. Of the 52% with indication for lipid lowering treatment (LLT), 44% were using LLT. The lipid goal attainment was 45% and 18% in the high and very high-risk group, respectively. Use of statins in monotherapy was 24%, while 1% used statins in combination with other LLT. Sixty-two % had hypertension and approximately half of these patients were at BP goal. The majority of the patients used antihypertensive treatment in monotherapy (24%), while 10% and 5% as a two- or three drug combination. CONCLUSION: We revealed considerable geographical differences in estimated CVD risk and preventive treatment. Low goal attainment for LLT was observed, and only half the patients obtained BP goal. Despite a high focus on the increased CVD risk in RA patients over the last decade, there is still substantial potential for improvement in CVD preventive measures.

[19] *Plakogiannis R, Sorbera M, Fischetti B, Chen M*. **The Role of Antisense Therapies Targeting Lipoprotein(a)**. Journal of cardiovascular pharmacology 2021; 78:e5-e11.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34232223

ABSTRACT

Atherosclerotic cardiovascular disease (ASCVD) continues to be the leading cause of preventable death in the United States. Elevated low-density lipoprotein cholesterol (LDL-C) is well known to result in cardiovascular disease. Mainstay therapy for reducing LDL-C and ASCVD risk is statin therapy. Despite achieving desired LDL-C levels with lipid-lowering therapy, cardiovascular residual risk often persists. Elevated lipoprotein(a) [Lp(a)] levels have been highlighted as an inherent independent predictor of ASCVD, and decreasing Lp(a) levels may result in a significant reduction in the residual risk in high-risk patients. To date, there are no approved medications to lower Lp(a) levels. Nicotinic acid, proprotein convertase subtilisin/kexin 9 inhibitors, and antisense oligonucleotide have demonstrated modest to potent Lp(a) reduction. Spotlight has been placed on antisense oligonucleotides and their role in Lp(a) lowering. APO(a)LRx is in the frontline for selectively decreasing Lp(a) concentrations and ongoing research may prove that this medication may lower Lp(a)-mediated residual risk, translating into cardiovascular benefit.

[20] *Patriki D, Saravi SSS, Camici GG et al.* **PCSK 9: A Link Between Inflammation and Atherosclerosis**. Curr Med Chem 2021.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34238141

ABSTRACT

Proprotein convertase subtilisin/Kexin 9 (PCSK 9) was revealed to be a key player in the lipid metabolism and therefore in the development and progression of atherosclerosis. PCSK 9 binds to the low-density lipoprotein (LDL) receptor, induces its degradation, and increases circulating blood LDL. As a result, PCSK 9 inhibitors represent an essential pillar in cardiovascular risk reduction therapies due to their highest good LDL decreasing properties. While the influence of PCSK 9 on lipid metabolism has been widely investigated, the full pathophysiological spectrum of PCSK 9 is yet to be determined. Statins have already been demonstrated to have beneficial anti-inflammatory effects. In this context, evidence suggests that PCSK 9 also interferes with inflammatory processes and thereby contributes to the development of atherosclerosis. As lipid metabolism on its own affects inflammatory processes, it is difficult to distinguish between lipid-dependent and -independent inflammatory properties of PCSK 9. A body of evidence has revealed that PCSK9 LDL-independently regulates the secretion of pro-inflammatory cytokines and inflammation-underlying pathways in vascular walls. In contrast, recent observations suggest that PCSK9 interacts with lectin-like oxidized LDL receptor-1 (LOX-1) and dampens inflammatory responses through LDL reduction. In conclusion, this review provides mounting evidence indicating how PCSK9 promotes vascular inflammation and subsequent atherosclerosis to shed light on the anti-inflammatory effects of PCSK9 inhibitors in preventing atherosclerosis.

[21] *Ng DS*. **Evolving ANGPTL-based lipid-lowering strategies and beyond**. Current opinion in lipidology 2021; 32:271-272.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34227579

ABSTRACT

[22] *Muchiri JW, Gericke GJ, Rheeder P*. **Effectiveness of an adapted diabetes nutrition education program on clinical status, dietary behaviors and behavior mediators in adults with**

type 2 diabetes: a randomized controlled trial. Journal of diabetes and metabolic disorders 2021; 20:293-306.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34222067

ABSTRACT

PURPOSE: This study evaluated the effectiveness of an adapted social-cognitive theory underpinned diabetes nutrition education program (NEP) on: clinical (HbA1c, BMI, blood lipids, blood pressure) and selected dietary behaviors (starchy foods and energy intake, vegetables and fruit intake) and behavior mediators (knowledge and diabetes management self-efficacy) in patients with type 2 diabetes mellitus (T2DM). METHODS: A tertiary hospital outpatient adults (40-70 years) with poorly controlled (HbA1c ≥ 8 %) T2DM were randomized to either intervention group (n = 39: NEP, 7-monthly group education sessions, bi-monthly follow-up sessions, 15-minute individual session, workbook + education materials) or control group (n = 38: education materials only). NEP aimed to improve clinical status through improved dietary behaviors and behavior mediators. Outcomes and changes in diabetes medication were assessed at six and 12 months. Intention-to-treat analysis was conducted. ANCOVA compared the groups (baseline values, age, sex adjustments). RESULTS: Forty-eight (62.3 %) participants completed the study. Intervention group compared to the control group had lower (-0.53 %), clinically meaningful HbA1c (primary outcome) at 6 months, albeit not sustained at 12 months. Compared to the control group, the intervention group had significantly lower: (i) systolic blood pressure at six and 12 months (ii) diastolic pressure at 12 months, (iii) energy intake at six-months, (iv) up-titration of insulin at six and 12 months and higher diabetes knowledge scores at six months. CONCLUSIONS: NEP had limited effects on HbA1c, targeted dietary behaviors and behavior mediators but showed positive effects on blood pressure. The NEP health cost savings potential supports the need for improving program participation. TRIAL REGISTRATION: ClinicalTrials.gov. number NCT03334773; 7 November 2017 retrospectively registered.

[23] *Lin Q, Fu Y, Zang X et al.* **The Role of Fasting LDL-C Levels in Their Non-fasting Reduction in Patients With Coronary Heart Disease**. Frontiers in cardiovascular medicine 2021; 8:686234.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34222380

ABSTRACT

The level of low-density lipoprotein cholesterol (LDL-C) decreases to a certain extent after daily meals; however, the influencing factor of this phenomenon has not been fully elucidated. This study included 447 patients with coronary heart disease (CHD). Serum levels of blood lipid parameters at 0, 2, and 4 hours (h) after a daily breakfast were monitored in all subjects. The levels of total cholesterol (TC), LDL-C, high-density lipoprotein cholesterol (HDL-C) and non-HDL-C significantly decreased, while those of triglycerides (TG) and remnant cholesterol (RC) significantly increased from baseline to 4 h in both male and female patients ($P < 0.05$). Multiple linear regression analysis showed that fasting LDL-C level, the non-fasting change in RC level at 4 h and fasting TG level were significant predictors of the non-fasting change in LDL-C level at 4 h in patients with CHD, and fasting LDL-C level was the most significantly associated with the non-fasting change in LDL-C level. Patients with lower levels of fasting LDL-C had smaller non-fasting changes in LDL-C levels. When the fasting LDL-C level was <1.4 mmol/L, both absolute reduction and percent reduction in LDL-C level at 4 h were almost zero, which means that the non-fasting LDL-C level at 4 h was approximately equivalent to its fasting value ($P < 0.05$). This result indicated that the non-fasting changes in LDL-C levels were

influenced by fasting LDL-C levels in patients with CHD. When the fasting LDL-C level was <1.4 mmol/L, the non-fasting LDL-C level could replace the fasting value to guide treatment.

[24] *Langer A, Mancini GBJ, Tan M et al.* **Treatment Inertia in Patients With Familial Hypercholesterolemia**. Journal of the American Heart Association 2021; 10:e020126.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34238023

ABSTRACT

Background We studied care gap in patients with familial hypercholesterolemia (FH) with respect to lipid-lowering therapy. Methods and Results We enrolled patients with cardiovascular disease (CVD) or FH and low-density lipoprotein-cholesterol >2.0 mmol/L despite maximally tolerated statin therapy. During follow-up physicians received online reminders of treatment recommendations of 2009 patients (median age, 63 years, 42% women), 52.4% had CVD only, 31.7% FH only, and 15.9% both CVD and FH. Patients with FH were younger and more likely to be women and non-White with significantly higher baseline low-density lipoprotein-cholesterol level (mmol/L) as compared with patients with CVD (FH 3.92±1.48 versus CVD 2.96±0.94, P<0.0001). Patients with FH received less statin (70.6% versus 79.2%, P=0.0001) at baseline but not ezetimibe (28.1% versus 20.4%, P=0.0003). Among patients with FH only, 45.3% were at low-density lipoprotein target (≥ 50% reduction from pre-treatment level or low-density lipoprotein <2.5 mmol/L) at baseline and increasing to 65.8% and 73.6% by visit 2 and 3, respectively. Among patients with CVD only, none were at recommended level (≤2.0 mmol/L) at baseline and 44.3% and 53.3% were at recommended level on second and third visit, respectively. When primary end point was analyzed as a difference between baseline and last available follow-up observation, only 22.0% of patients with FH only achieved it as compared with 45.8% with CVD only (P<0.0001) and 55.2% with both FH+CVD (P<0.0001). Conclusions There is significant treatment inertia in patients with FH including those with CVD. Education focused on patients with FH should continue to be undertaken.

[25] *Jayatilaka S, Desai K, Rijal S, Zimmerman D*. **Statin-Induced Autoimmune Necrotizing Myopathy**. J Prim Care Community Health 2021; 12:21501327211028714.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34219515

ABSTRACT

Statin therapy is a widely prescribed medication class for hypercholesterolemia. In statin-induced autoimmune myopathy, genetically predisposed and at-risk patients can develop antibodies against hydroxy-3-methylglutaryl-CoA reductase (HMGCR), the key enzyme in the production of cholesterol. As a result, an autoimmune reaction causing weakness, myalgia, with possible severe rhabdomyolysis, renal failure, and myonecrosis also can occur. A 73-year-old female presented to clinic with myalgia and fatigue. She was on atorvastatin 20 mg/day for over 1 year, which she stopped 1 week prior to her initial presentation. Patient did experience rhabdomyolysis as well as a transaminitis. She underwent an autoimmune workup which was positive for HMG-CoA reductase antibodies. Patient was initially treated on a prednisone taper, starting dose 50 mg/day. Without remission of symptoms, methotrexate 15 mg/week was initiated.

[26] *Iqbal T, Miller M*. **A Fishy Topic: VITAL, REDUCE-IT, STRENGTH, and Beyond: Putting Omega-3 Fatty Acids into Practice in 2021**. Current cardiology reports 2021; 23:111.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34247311

ABSTRACT
PURPOSE OF REVIEW: To examine recently published data from clinical outcome and arteriographic studies that examined the addition of omega-3 fatty acids, eicosapentaenoic acid (EPA) + docosahexanoic acid (DHA), to standard of care therapy on cardiovascular disease (CVD) risk. RECENT FINDINGS: Several trials that tested purified EPA (JELIS, REDUCE-IT, EVAPORATE) were associated with reduced CVD risk and regression of low attenuation coronary plaque volume, whereas studies that employed the combination EPA/DHA (VITAL, OMEMI, STRENGTH) failed to derive clinical benefit. Trials testing purified EPA consistently demonstrated reduction in atheromatous volume or CVD events beyond standard of care therapies, whereas the combination of EPA/DHA did not, despite producing similar reductions in triglycerides. Experimental and in vitro data suggest that compared to DHA, EPA exhibits antioxidant, anti-inflammatory, and membrane stabilizing properties that enhance vascular function and CVD risk. Consequently, purified EPA appears to be the treatment of choice for high-risk patients with hypertriglyceridemia.

[27] *Geng L, Du P, Yuan Y et al.* **Impact of Arterial Remodeling of Intermediate Coronary Lesions on Long-Term Clinical Outcomes in Patients with Stable Coronary Artery Disease: An Intravascular Ultrasound Study**. J Interv Cardiol 2021; 2021:9915759.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34220369

ABSTRACT
BACKGROUND: Treatment of coronary intermediate lesions remains a controversy, and the role of arterial remodeling patterns determined by intravascular ultrasound in intermediate lesion is still not well known. The aim of this study was to investigate the impact of arterial remodeling of intermediate coronary lesions on long-term clinical outcomes. METHODS: Arterial remodeling patterns were assessed in 212 deferred intermediate lesions from 162 patients after IVUS examination. Negative, intermediate, and positive remodeling was defined as a remodeling index of <0.88, 0.88~1.0, and >1.0, respectively. The primary endpoint was the composite vessel-oriented clinical events, defined as the composition of target vessel-related cardiac death, target vessel-related myocardial infarction, and target vessel revascularization. Quantitative flow ratio was assessed for evaluating the functional significance of intermediate lesions. RESULTS: 72 intermediate remodeling lesions were present in 66 patients, whereas 77 negative remodeling lesions were present in 71 patients, and 63 positive remodeling lesions were present in 55 patients. Negative remodeling lesions had the smallest minimum lumen area (4.16 ± 1.03 mm(2) vs. 5.05 ± 1.39 mm(2) vs. 4.85 ± 1.76 mm(2); $P < 0.01$), smallest plaque burden (63.45 ± 6.13% vs. 66.12 ± 6.82% vs. 71.17 ± 6.45%; $P < 0.01$), and highest area stenosis rate (59.32% ± 10.15% vs. 54.61% ± 9.09% vs. 51.67% ± 12.96%; $P < 0.01$). No significant difference was found in terms of quantitative flow ratio among three groups. At 5 years follow-up, negative remodeling lesions had a higher rate of composite vessel-oriented clinical event (14.3%), compared to intermediate (1.4%, P=0.004) or positive remodeling lesions (4.8%, P=0.06). After adjusting for multiple covariates, negative remodeling remained an independent determinant for vessel-oriented clinical event (HR: 4.849, 95% CI 1.542-15.251, P=0.007). CONCLUSION: IVUS-derived negative remodeling is associated with adverse long-term clinical outcome in stable patients with intermediate coronary artery stenosis.

[28] *Dong Y, Liu X, Zhao Y et al.* **Attenuating the Variability of Lipids Is Beneficial for the Hypertension Management to Reduce the Cardiovascular Morbidity and Mortality in Older Adults**. Frontiers in cardiovascular medicine 2021; 8:692773.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34222383

ABSTRACT

Objective: To investigate the beneficial of attenuating the variability of lipids to the hypertension management in older adults. Methods: Between April 2008 and November 2010, 1,244 hypertensive patients aged ≥60 years were recruited and randomized into placebo and rosuvastatin groups. Outcomes and inter-visit plasma lipids variability were assessed. Results: Over an average follow-up of 83.5 months, the coefficients of variation (CVs) in total cholesterol (TCHO), triglycerides, high-density lipoprotein cholesterol (HDL-c), and low-density lipoprotein cholesterol (LDL-c) were significantly lower in the rosuvastatin group than the placebo group ($p < 0.05$). The risks of composite cardiovascular event, myocardial infarction, coronary revascularization, heart failure, total stroke, ischemic stroke, cardiovascular death, and all-cause death were significantly lower in the rosuvastatin group than the placebo group (all $p < 0.05$). The differences in the risks were significantly diminished after the CVs for TCHO, triglycerides, HDL-c, and LDL-c were separately included as confounders. One-SD of CVs for TCHO, triglycerides, HDL-c, and LDL-c increment were significantly associated with the risks of composite cardiovascular event, myocardial infarction, heart failure, total stroke, ischemic stroke, cardiovascular death, and all-cause death, respectively (all $p < 0.05$). Conclusions: Rosuvastatin significantly attenuated the intra-visit variability in lipids and decreased the risk of cardiovascular mortality and morbidity. Controlling the variability of lipids is as important as antihypertensive treatment to reduce the cardiovascular morbidity and mortality in the management of older hypertensive patients. Clinical Trial Registration: ChiCTR.org.cn, ChiCTR-IOR-17013557.

[29] *Choi J, Kim H, Jun J et al.* **Recurrent Pancreatitis in a Pregnant Woman with Severe Hypertriglyceridemia Successfully Managed by Multiple Plasmapheresis**. Journal of atherosclerosis and thrombosis 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34219115

ABSTRACT

Hypertriglyceridemia (HTG) is a state of increased serum triglyceride (TG) affected by multigenetic and multifactorial causes. Serum TG concentration can be markedly elevated if exposed to precipitating factors, such as estrogen hormone and pregnancy. We report the case of a patient with severe HTG who suffered from recurrent pancreatitis during the second trimester of pregnancy conceived with in vitro fertilization-embryo transfer (IVF-ET) and was successfully controlled by multiple sessions of plasmapheresis.A 24-year-old pregnant woman was admitted because of a sudden onset of severe abdominal pain at 26 weeks of gestation conceived by IVF-ET. She has experienced recurrent pancreatitis despite low-fat diet and dyslipidemia medications allowed in pregnancy. At admission, serum amylase and lipase were elevated to 347 and 627 U/L, respectively, along with fasting TG to 4809 mg/dL. A clinical diagnosis of HTG-induced acute pancreatitis was made, and plasmapheresis was performed. After plasmapheresis, serum TG, amylase, and lipase levels decreased to 556 mg/dL, 60 U/L, and 69 U/L, respectively, along with subsequent pain relief. The patient underwent a total of nine sessions of plasmapheresis to retain serum TG lower than 1,000 mg/dL during pregnancy, with no further recurrence of acute pancreatitis. After delivery, the serum TG level was maintained below 500 mg/dL with a combination treatment of fenofibrate, statin,

and ezetimibe.Although severe HTG is usually asymptomatic, if exposed to precipitating factors, it can cause acute pancreatitis, a fatal complication. Early application of plasmapheresis may be a useful option in HTG-induced acute pancreatitis intractable to medical treatment; however, its indications, risks, and benefits should be carefully evaluated.

[30] *Chidambaram V, Zhou L, Ruelas Castillo J et al.* **Higher Serum Cholesterol Levels Are Associated With Reduced Systemic Inflammation and Mortality During Tuberculosis Treatment Independent of Body Mass Index**. Frontiers in cardiovascular medicine 2021; 8:696517.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34239907

ABSTRACT

Background: Lipids play a central role in the pathogenesis of tuberculosis (TB). The effect of serum lipid levels on TB treatment (ATT) outcomes and their association with serum inflammatory markers have not yet been characterized. Methods: Our retrospective cohort study on drug-susceptible TB patients, at the National Taiwan University Hospital, assessed the association of baseline serum lipid levels such as low-density lipoprotein (LDL), high-density lipoprotein (HDL), total cholesterol (TC) and triglycerides (TG) with all-cause and infection-related mortality during first 9 months of ATT and baseline inflammatory markers namely C-reactive protein (CRP), total leukocyte count (WBC), and neutrophil-lymphocyte ratio (NL ratio). Results: Among 514 patients, 129 (26.6%) died due to any-cause and 72 (14.0%) died of infection. Multivariable Cox-regression showed a lower adjusted hazard ratio (aHR) of all-cause mortality in the 3rd tertiles of HDL (aHR 0.17, 95% CI 0.07-0.44) and TC (aHR 0.30, 95% CI 0.14-0.65), and lower infection-related mortality in the 3rd tertile of HDL (aHR 0.30, 95% CI 0.14-0.65) and TC (aHR 0.30, 95% CI 0.14-0.65) compared to the 1st tertile. The 3rd tertiles of LDL and TG showed no association in multivariable analysis. Similarly, 3rd tertiles of HDL and TC had lower levels of baseline inflammatory markers such as CRP, WBC, and NL ratio using linear regression analysis. Body mass index (BMI) did not show evidence of confounding or effect modification. Conclusions: Higher baseline serum cholesterol levels were associated with lower hazards of all-cause and infection-related mortality and lower levels of inflammatory markers in TB patients. BMI did not modify or confound this association.

[31] *Tian Q, Corkum AE, Moaddel R, Ferrucci L*. **Metabolomic profiles of being physically active and less sedentary: a critical review**. Metabolomics : Official journal of the Metabolomic Society 2021; 17:68.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34245373

ABSTRACT

BACKGROUND: Being physically active has multiple salutary effects on human health, likely mediated by changes in energy metabolism. Recent reviews have summarized metabolomic responses to acute exercise. However, metabolomic profiles of individuals who exercise regularly are heterogeneous. AIM OF REVIEW: We conducted a systematic review to identify metabolites associated with physical activity (PA), fitness, and sedentary time in community-dwelling adults and discussed involved pathways. Twenty-two studies were eligible because they (1) focused on community-dwelling adults from observational studies; (2) assessed PA, fitness, and/or sedentary time, (3) assessed metabolomics in biofluid, and (4) reported on relationships of metabolomics with PA, fitness, and/or sedentary time. KEY SCIENTIFIC CONCEPTS OF REVIEW: Several metabolic pathways were associated with higher PA and fitness and less sedentary time, including tricarboxylic

acid cycle, glycolysis, aminoacyl-tRNA biosynthesis, urea cycle, arginine biosynthesis, branch-chain amino acids, and estrogen metabolism. Lipids were strongly associated with PA. Cholesterol low-density lipoproteins and triglycerides were lower with higher PA, while cholesterol high-density lipoproteins were higher. Metabolomic profiles of being physically active and less sedentary indicate active skeletal muscle biosynthesis supported by enhanced oxidative phosphorylation and glycolysis and associated with profound changes in lipid and estrogen metabolism. Future longitudinal studies are needed to understand whether these metabolomic changes account for health benefits associated with PA.

[32] *Semb AG, Rollefstad S, Ikdahl E et al.* **Diabetes mellitus and cardiovascular risk management in patients with rheumatoid arthritis: an international audit**. RMD Open 2021; 7.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34244381
ABSTRACT
AIM: The objective was to examine the prevalence of atherosclerotic cardiovascular disease (ASCVD) and its risk factors among patients with RA with diabetes mellitus (RA-DM) and patients with RA without diabetes mellitus (RAwoDM), and to evaluate lipid and blood pressure (BP) goal attainment in RA-DM and RAwoDM in primary and secondary prevention. METHODS: The cohort was derived from the Survey of Cardiovascular Disease Risk Factors in Patients with Rheumatoid Arthritis from 53 centres/19 countries/3 continents during 2014-2019. We evaluated the prevalence of cardiovascular disease (CVD) among RA-DM and RAwoDM. The study population was divided into those with and without ASCVD, and within these groups we compared risk factors and CVD preventive treatment between RA-DM and RAwoDM. RESULTS: The study population comprised of 10 543 patients with RA, of whom 1381 (13%) had DM. ASCVD was present in 26.7% in RA-DM compared with 11.6% RAwoDM ($p<0.001$). The proportion of patients with a diagnosis of hypertension, hyperlipidaemia and use of lipid-lowering or antihypertensive agents was higher among RA-DM than RAwoDM ($p<0.001$ for all). The majority of patients with ASCVD did not reach the lipid goal of low-density lipoprotein cholesterol <1.8 mmol/L. The lipid goal attainment was statistically and clinically significantly higher in RA-DM compared with RAwoDM both for patients with and without ASCVD. The systolic BP target of <140 mm Hg was reached by the majority of patients, and there were no statistically nor clinically significant differences in attainment of BP targets between RA-DM and RAwoDM. CONCLUSION: CVD preventive medication use and prevalence of ASCVD were higher in RA-DM than in RAwoDM, and lipid goals were also more frequently obtained in RA-DM. Lessons may be learnt from CVD prevention programmes in DM to clinically benefit patients with RA .

[33] *Miksenas H, Januzzi JL, Jr., Natarajan P*. **Lipoprotein(a) and Cardiovascular Diseases**. Jama 2021; 326:352-353.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34236417
ABSTRACT

[34] *Maggioni AP, Dondi L, Andreotti F et al.* **Prevalence, prescriptions, outcomes and costs of type 2 diabetes patients with or without prior coronary artery disease or stroke: a longitudinal 5-year claims-data analysis of over 7 million inhabitants**. Therapeutic advances in chronic disease 2021; 12:20406223211026390.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34221306

ABSTRACT
AIMS: To analyze the prevalence, comorbidities, outcomes and costs of type 2 diabetes mellitus (T2DM) patients with and without coronary artery disease (CAD) or stroke in a population of over 7 million inhabitants. METHODS: T2DM patients were identified in 2015 (accrual period) from the Ricerca e Salute (ReS) database linking administrative records to demographics. Based on 2013-2015 information, four cohorts were considered: #1 with CAD and/or stroke; #2 without CAD and/or stroke; #3 with chronic CAD but no myocardial infarction or stroke; #4 with chronic CAD undergoing percutaneous coronary interventions (PCI). Hospitalizations, drugs and other outpatient care were assessed from 2015 to 2017. RESULTS: The prevalence of T2DM was 6% (441,085/7,365,954). CAD and/or stroke in the previous 3 years affected 7.5% of T2DM patients (33,153); this cohort was generally older, of male sex, with more comorbidities, prescriptions, and hospital admissions (50.5% versus 13.4% during the first follow-up year) compared to cohort #2. Yearly costs were over three-fold for cohort #1 versus #2, main drivers being hospitalizations in the former and drugs in the latter. Two-year cardiovascular events were recorded significantly more commonly in cohort #4 compared to the other cohorts. Guideline-recommended lipid-lowering therapy was <80% in all but cohort #4. CONCLUSIONS: The present analysis points to three areas of potential improvement in T2DM management: (a) guideline-recommended treatment patterns of T2DM patients; (b) three-fold recurrences and costs in T2DM patients with, compared to those without, prior cardiovascular events; (c) high event rates associated with chronic CAD and PCI, warranting specific studies aimed at improved prevention.

[35] *Lu Y, Ye MF, Zhao JJ et al.* **Gadolinium enhancement of atherosclerotic plaque in the intracranial artery**. Neurol Res 2021:1-10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34229565

ABSTRACT
Background: Gadolinium enhancement on high resolution magnetic resonance imaging (HR-MRI) has been considered a sign of instability and inflammation of intracranial atherosclerotic plaques. Our research objective was to explore the relationship between the extent of plaque enhancement (PE), the degree of intracranial artery stenosis, and acute ischemic stroke events.Methods: HR-MRI was performed in 91 patients with intracranial vascular stenosis to determine the existence and intensity of PE.Results: Among 91 patients enrolled in the trial, there were 43 patients in the acute/subacute group (≤1 month from ischemic stroke event), 15 patients in the chronic group (>1 month from ischemic stroke event), and 33 patients in the non-culprit plaques group (no ischemic stroke event). A total of 105 intracranial atherosclerotic plaques were detected in 91 patients. 14 (13.3%) were mild-stenosis plaques, 22 (21.0%) were moderate-stenosis plaques, and 69 (65.7%) were severe-stenosis plaques. There were 12 (11.4%), 18 (17.1%), and 75 (71.4%) plaques in the non-enhanced plaque group, the mild-enhancement group, and the significant-enhancement group, respectively. The degree of PE among the acute/subacute group, the chronic group, and the non-culprit plaque group had a significant difference (P = 0.005). Enhanced plaques were more often observed in culprit plaques (acute/subacute group and chronic group) than non-culprit plaques (96.7% vs 77.3%). Non-enhanced plaques were more often observed in non-culprit plaques than culprit plaques (acute/subacute group and chronic group) (22.7% vs 3.3%). And 36.6% of the enhanced plaques were non-culprit plaques. After performing univariate and multivariate logistic regression analysis, the results showed that strong plaque enhancement (P = 0.025, odds ratio [OR] 3.700, 95% confidence

interval [95% CI] 1.182-11.583) and severe stenosis (P = 0.008, OR 4.393, 95%CI 1.481-13.030) were significantly associated with acute ischemic events.Conclusion: Enhanced plaques were more often observed in culprit plaques, and non-enhanced plaques were more often observed in non-culprit plaques. Moreover, significant plaque enhancement and severe ICAS were closely associated with acute ischemic events.

[36] *Lin M, Xu T, Zhang W et al.* **Effect of statins on post-contrast acute kidney injury: a multicenter retrospective observational study**. Lipids in health and disease 2021; 20:63.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34225750

ABSTRACT

BACKGROUND: Post-contrast acute kidney injury (PC-AKI) is a severe complication of coronary angiography (CAG) and percutaneous coronary intervention (PCI). Currently, the effect of statins on PC-AKI and its mechanism remains unclear. METHODS: This multicenter retrospective observational study included 4386 patients who underwent CAG or PCI from December 2006 to December 2019 in Sir Run Run Shaw Hospital and its medical consortium hospitals. Serum creatinine pre- or post-procedure within 72 h after PCI was recorded. Multivariate logical regression was used to explore whether preoperative use of statins was protective from PC-AKI. The path analysis model was then utilized to look for the mediation factors of statins. RESULTS: Four thousand three hundred eighty-six patients were enrolled totally. The median age of the study population was 68 years old, 17.9% with PC-AKI, and 83.3% on preoperative statins therapy. The incidence of PC-AKI was significantly lower in group of patients on statins therapy. Multivariate regression indicated that preoperative statins therapy was significantly associated with lower percentage of elevated creatinine (β: -0.118, P < 0.001) and less PC-AKI (OR: 0.575, P < 0.001). In the preoperative statins therapy group, no statistically significant difference was detected between the atorvastatin and rosuvastatin groups (OR: 1.052, P = 0.558). Pathway model analysis indicated a direct protective effect of preoperative statins therapy on PC-AKI (P < 0.001), but not through its lipid-lowering effect (P = 0.277) nor anti-inflammatory effect (P = 0.596). Furthermore, it was found that "low-density lipoprotein cholesterol (LDL-C)→C-reactive protein (CRP)" mediated the relationship between preoperative statins therapy and PC-AKI (P = 0.007). However, this only explained less than 1% of the preoperative protective effects of statins on PC-AKI. CONCLUSION: Preoperative statins therapy is an independent protective factor of PC-AKI, regardless of its type. This protective effect is not achieved by lipid-lowering effect or anti-inflammatory effect. These findings underscore the potential use of statins in preventing PC-AKI among those at risk.

[37] *Lin CH, Huang RY, Lu TP et al.* **High prevalence of APOA1/C3/A4/A5 alterations in luminal breast cancers among young women in East Asia**. NPJ Breast Cancer 2021; 7:88.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34226567

ABSTRACT

In East Asia, the breast cancer incidence rate among women aged <50 years has rapidly increased. Emerging tumors are distinctly characterized by a high prevalence of estrogen receptor (ER)-positive/human epidermal growth factor receptor (HER2)-negative cancer. In the present study, we identified unique genetic alterations in these emerging tumors. We analyzed gene copy number variations (CNVs) in breast tumors from 120 Taiwanese patients, and obtained public datasets of CNV and gene expression (GE). The data regarding CNV and GE were separately compared

between East Asian and Western patients, and the overlapping genes identified in the comparisons were explored to identify the gene-gene interaction networks. In the age <50 years/ER+/HER2- subgroup, tumors of East Asian patients exhibited a higher frequency of copy number loss in APOA1/C3/A4/A5, a lipid-metabolizing gene cluster (33 vs. 10%, P<.001) and lower APOA1/C3/A4/A5 expressions than tumors of Western patients. These copy number loss related- and GE-related results were validated in another Taiwanese cohort and in two GE datasets, respectively. The copy number loss was significantly associated with poor survival among Western patients, but not among East Asian patients. Lower APOA1, APOC3, and APOA5 expressions were associated with higher ESTIMATE immune scores, indicating an abundance of tumor-infiltrating immune cells. In conclusion, APOA1/C3/A4/A5 copy number loss was more prevalent in luminal breast tumors among East Asian women aged <50 years, and its immunomodulatory effect on the tumor microenvironment possibly plays various roles in the tumor biology of East Asian patients.

[38] *Li ZM, Wang MJ*. **[Current studies of cytokines in the pathogenesis of atherosclerosis and its therapeutic measures]**. Sheng li xue bao : [Acta physiologica Sinica] 2021; 73:501-508.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34230951

ABSTRACT

Atherosclerosis is a chronic inflammatory disease. Cytokine-related research provides an important direction for the prevention and treatment of atherosclerosis. Cytokines, produced by different types of cells and acting on a range of targets, play a key role in the pathogenesis and progression of atherosclerosis. This review summarizes the main pro-inflammatory and anti-inflammatory cytokines related to atherosclerosis and their underlying mechanism. We also outline current anti-atherosclerosis treatments targeting cytokines. The research and treatment prospects of cytokines in the prevention and treatment of atherosclerosis are discussed briefly as well.

[39] *Li Y, Gu Y, Jin Y, Mao Z*. **Is Bariatric Surgery Effective for Chinese Patients with Type 2 Diabetes Mellitus and Body Mass Index < 35 kg/m(2)? A Systematic Review and Meta-analysis**. Obesity surgery 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34244912

ABSTRACT

BACKGROUND: Bariatric surgery has been applied for weight loss and comorbidity control in China since 2000. Recent studies have shown positive results for bariatric surgery in patients with a body mass index (BMI) of less than 35 kg/m(2). However, the effect of surgery on Chinese patients with type II diabetes mellitus (T2DM) has not yet been systematically investigated. METHODS: A comprehensive literature search was performed in the Cochrane Library, Embase, PubMed, and Web of Science from January 2014 to March 2020. All studies examined bariatric surgery outcomes on Chinese patients at 12-, 36-, and 60-month follow-up. The research followed the guidance of Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) recommendations. RESULTS: Eleven studies containing 611 patients were included in this meta-analysis. Clinical indices at 12-, 36-, and 60-month follow-up were analyzed. Significant decreases were identified in body weight, BMI, waist circumference (WC), blood pressure (BP), fasting plasma glucose (FPG), glycosylated hemoglobin A1c (hemoglobin A1c, or HbA1c), triglyceride (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) postoperatively. An increasing trend in the T2DM remission rate was discovered. The remission group was observed to have significantly

lower HbA1c and C-peptide level, a shorter duration of T2DM, and a higher BMI than the nonremission group at 12 months. CONCLUSIONS: Bariatric surgery successfully provided significant BMI control as well as a reduction and normalization of glucose- and lipid-related metabolism at 12, 36, and 60 months postoperatively in Chinese patients with T2DM with a preoperative BMI of less than 35 kg/m(2). An increasing trend in the T2DM remission rate suggested promising future applications in this population.

[40] *Jung SW, Moon JY*. **The role of inflammation in diabetic kidney disease**. The Korean journal of internal medicine 2021; 36:753-766.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34237822

ABSTRACT

Diabetic kidney disease (DKD) has been the leading cause of chronic kidney disease for over 20 years. Yet, over these two decades, the clinical approach to this condition has not much improved beyond the administration of glucose-lowering agents, renin-angiotensin-aldosterone system blockers for blood pressure control, and lipid-lowering agents. The proportion of diabetic patients who develop DKD and progress to end-stage renal disease has remained nearly the same. This unmet need for DKD treatment is caused by the complex pathophysiology of DKD, and the difficulty of translating treatment from bench to bed, which further adds to the growing argument that DKD is not a homogeneous disease. To better capture the full spectrum of DKD in our design of treatment regimens, we need improved diagnostic tools that can better distinguish the subgroups within the condition. For instance, DKD is typically placed in the broad category of a non-inflammatory kidney disease. However, genome-wide transcriptome analysis studies consistently indicate the inflammatory signaling pathway activation in DKD. This review will utilize human data in discussing the potential for redefining the role of inflammation in DKD. We also comment on the therapeutic potential of targeted anti-inflammatory therapy for DKD.

[41] *Chowdhury JA, Nessa A, Nessa W et al.* **Association of Hypertension and Hypercholesterolemia in Patients with Type-2 Diabetes Mellitus**. Mymensingh medical journal : MMJ 2021; 30:651-656.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34226451

ABSTRACT

The present cross-sectional analytical study was carried out to observe blood pressure and serum total cholesterol in patients with type-2 diabetes mellitus. This observational study was carried out in the department of Physiology, Mymensingh Medical College, Mymensingh, Bangladesh from January 2016 to December 2016. For this purpose, 200 subjects of both sexes and age ranged from 30-60 years were selected; among them 100 were type-2 diabetic person and 100 were apparently healthy. Blood pressure and serum total cholesterol was significantly higher ($p<0.0001$) in both male and female of the study group in comparison to healthy control group. From this study, it may conclude that type-2 persons are considered to have significant positive relation for formation of hypertension, hypercholesterolemia and metabolic abnormalities that have high morbidity and mortality. So, prevention of type-2 diabetes mellitus by taking necessary steps like regular physical exercise, intake of healthy diet and behavior therapy may help in prevention of type-2 diabetes mellitus related complication.

[42] *Choi WM, Kim HJ, Jo AJ et al.* **Association of aspirin and statin use with the risk of liver cancer in chronic hepatitis B: A nationwide population-based study**. Liver international : official journal of the International Association for the Study of the Liver 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34242482

ABSTRACT
BACKGROUND & AIMS: Aspirin and statins have been suggested to prevent hepatocellular carcinoma (HCC). However, the combined effects of aspirin and statins on HCC risk in patients with chronic hepatitis B (CHB) are not clear. METHODS: A nationwide nested case-control study was performed with data from the National Health Insurance Service gathered between 2005 and 2015 in Korea. In a cohort of 538,135 treatment-naïve, non-cirrhotic patients with CHB, 6,539 HCC cases were matched to 26,156 controls and were analysed by conditional logistic regression. Separate historical cohort studies for each drug were analysed by time-dependent Cox regression as a sensitivity analysis. RESULTS: In the nested case-control study, statins (OR 0.34; 95% CI 0.32-0.37) and aspirin (OR 0.92; 95% CI 0.85-0.99) were significantly associated with a HCC risk reduction. However, dose-dependent risk reduction was observed only with statins. By sensitivity analysis in the historical cohorts, statin users (n = 244,455; HR 0.67; 95% CI 0.66-0.68) and aspirin users (n = 288,777; HR 0.81; 95% CI 0.80-0.82) had significantly lower HCC risk. In the drug-stratified analyses, statins were associated with significantly reduced risk of HCC regardless of aspirin, whereas aspirin did not show such associations. CONCLUSIONS: In this nationwide population-based study of patients with CHB, statin use was consistently associated with a significant and dose-dependent reduction in HCC risk. In contrast, the association between aspirin use and HCC risk reduction was not dose-dependent and was suggested to be confounded by statins.

[43] *Xu X, Hua Y, Liu B et al.* **Correlation Between Calcification Characteristics of Carotid Atherosclerotic Plaque and Plaque Vulnerability**. Therapeutics and clinical risk management 2021; 17:679-690.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34234444

ABSTRACT
PURPOSE: To investigate the relationship between calcification characteristics of carotid atherosclerotic plaque and lipid rich necrotic core (LRNC) and intraplaque hemorrhage (IPH). METHODS: Patients with severe carotid stenosis undergoing carotid endarterectomy (CEA) were selected. Ultrasound and CT angiography (CTA) were performed to evaluate the calcification characteristics of the plaque before the surgery. RESULTS: A total of 142 patients were included and 142 pathological specimens of postoperative plaque were obtained accordingly. There were 78 plaques (54.9%) with LRNC and 41 (28.9%) with IPH. The plaque with LRNC had higher calcification rate (93.6%) compared with the plaque with IPH (87.8%). LRNC was often found in multiple calcification ($P = 0.003$) and mixed type calcification ($P = 0.001$). Multiple calcification was more likely to combine with IPH ($P = 0.008$), while simple basal calcification was not likely to combine IPH ($P = 0.002$). Smaller granular calcification was more likely to be associated with IPH ($P < 0.05$). In multivariate regression analysis of IPH and calcification characteristics, simple basal calcification was still a protective factor for IPH (OR, 0.25; 95% CI, 0.09-0.66; $P = 0.005$), while multiple calcification was closely related to the occurrence of IPH (OR, 3.58; 95% CI, 1.49-8.61; $P = 0.004$). CONCLUSION: Calcification characteristics of carotid atherosclerotic plaques are closely related to the vulnerability of plaques, especially multiple calcification and mixed type calcification.

[44] *Leutner M, Matzhold C, Bellach L et al.* **Increase in testosterone levels is related to a lower risk of conversion of prediabetes to manifest diabetes in prediabetic males**. Wien Klin Wochenschr 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34223999

ABSTRACT

BACKGROUND: Testosterone plays an important role in the regulation of glucose metabolism. While earlier studies have shown that it has a protective effect in males, unfavorable effects of testosterone on glucose metabolism have been reported in females; however, whether there is a sex-specific relationship between testosterone and glucose metabolism in patients with prediabetes has not been investigated in detail hitherto. METHODS: This cross-sectional analysis investigated 423 males and 287 females with diagnosed prediabetes. Detailed assessment of their metabolic profiles was performed, including a 2-h oral glucose tolerance test (OGTT), HbA1c levels, calculation of insulin resistance with homeostatic model assessment for insulin resistance (HOMA-IR), assessment of lipid metabolism, anthropometric parameters and the fatty liver index (FLI). By using Spearman's correlation test, we investigated the sex-specific relationship between testosterone and metabolism in the prediabetic individuals. RESULTS: In the present study, prediabetic females (mean age 58.6 years, confidence interval [CI: 57.6 y; 59.5 y]) were characterized by lower fasting plasma glucose levels (104.2 mg/dl [CI: 103.0 mg/dl; 105.4 mg/dl] vs. 106.9 mg/dl [CI: 106.0 mg/dl; 107.8 mg/dl]) and a lower FLI (49.5 [CI: 45.7; 53.2] vs. 58.8 [CI: 55.8; 61.8]), but presented with a higher risk of developing manifest type 2 diabetes in the next 10 years (FINDRISK score: 17.6 [CI: 17.1; 18.1] vs. 16.1 [CI: 15.7; 16.5]) when compared to prediabetic males (mean age: 58.04 years [CI: 57.0 y; 59.1 y]). Testosterone was negatively related to insulin resistance (HOMA-IR: Spearman's ρ: -0.33, $p<0.01$), 2-h stimulated glucose levels during the OGTT ($\rho=-0.18$, $p<0.01$), HbA1c levels ($\rho=-0.13$, $p<0.05$), FLI and BMI in prediabetic males; however, no relationship between testosterone and metabolic parameters could be found in prediabetic females. CONCLUSION: The increase of testosterone levels in males was related to a more favorable glucose metabolism, including lower HbA1c, lower stimulated glucose levels and higher insulin sensitivity; however, in prediabetic females, testosterone was not related to glucose metabolism.