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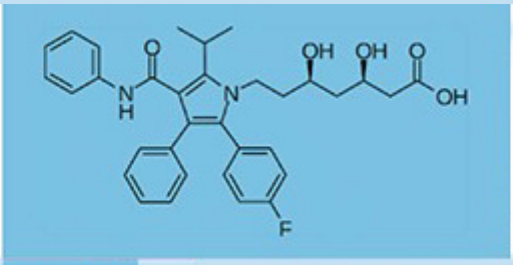
IAS STATIN NEWSLETTER



INTERNATIONAL ATHEROSCLEROSIS SOCIETY

A CURATED WEEKLY UPDATE OF ALL STATIN PUBLICATIONS

Update - Week 42, 2020

**Curated by Peter Lansberg,
a Dutch lipidologist and educator, and
reviewed by prof. Philip Barter, Past President of the
International Atherosclerosis Society.**

The IAS statin literature update will keep you up-to-date with all recent statin publications, using a curated approach to select relevant articles.

Key publications

Statin use associated with impressive improvements in NAFLD/NASH scores

NAFLD/NASH are recognized as an important global health care challenge. Prevalence in general populations has increased alarmingly in both developed- and developing economies. In the US, it is estimated that NAFLD affects 30-40% of the population, and in Indonesia, NAFLD has increased from 7.9% to 51% over the last 10-years. In this study, conducted in Greek military personnel during their annual medical check-up, both prevalence and the effects of three different statins were evaluated. Overall, 5400 soldiers participated in the initial screening. NAFLD/NASH was diagnosed in 613 participants. Patients were randomized to 4 treatment arms: diet-exercise, atorvastatin, rosuvastatin, and pitavastatin.

After 1-year, patients were re-evaluated using two non-invasive scores: the NAFLD Activity Score (NAS) and the Fibrosis-4 score (FIB-4). Only diet and exercise were not associated with any significant changes in both scores; NAS: 4.98 baseline vs. 5.62, (p=0.07); FIB-4: 3.42 vs. 3.52 (p=0.7). Patients that used atorvastatin, NAS: 4.97 vs 1.95, (p<0.001), FIB-4: 3.56 vs 0.83, (p<0.001. For rosuvastatin, NAS: 5.55 vs 1.81 (p<0.001), FIB-4: 3.61 vs 0.79 (p<0.001). And in patients that were allocated to pitavastatin, NAS: 4.89 vs 1.99 (p<0.001), FIB-4: 3.78 vs 0.87 (p<0.001). All three studied statins were associated with significant improvements in the two scores, compared to lifestyle intervention. This study's findings provide important insights into the benefits of statins in NAFLD/NASH patients. They are in line with Mendelian randomization studies' earlier findings that suggested that lipids are relevant mediators of both CVD and NAFLD risk. Current findings, in the context of earlier studies that presented similar results, statins should be considered an important pharmacological therapy to reduce CVD risk and improve NAFLD/NASH.

Sfikas G, Psallas M, Koumaras C *et al.* Prevalence, diagnosis and treatment with 3 different statins of non-alcoholic fatty liver disease/non-alcoholic steatohepatitis in military

personnel. Do genetics play a role? Current vascular pharmacology **2020. http://www.ncbi.nlm.nih.gov/pubmed/?term=33059580**

In Chinese post AMI patients; 20 mg vs 10 mg of rosuvastatin

The impact of rosuvastatin on post-AMI cardiac remodeling was evaluated in a small Chinese study of 93 patients. A low dose of 10 mg (N=46) was compared to the effects of 20 mg (N=47). The following parameters were evaluated at baseline and after 8 weeks of therapy. Blood lipid (TC, TG, LDL-C, and HDL-C), serum inflammatory markers (hs-CRP, IL-6, TNF-α and ICAM-1), ventricular remodeling markers (NT-pro BNP, MMP-9, TIMP-4, and Gal-3) and indicators of cardiac function (LVESD, LVESD, LVESV, LVEDV, IVST, and LVEF). Patients that used the higher dose of rosuvastatin experienced significant superior reductions in TC, TG, LDL-C, hs-CRP, IL-6, TNF-α, ICAM-1, NT-pro BNP, MMP-9, and Gal-3 (P<0.05). In combination with superior increases in HDL-C and TIMP-4 (P<0.05). Ejection fractions were increased (P<0.05), and echographic parameters for LVESD, LVESD, LVESV, LVEDV, and IVST were significantly better (P< 0.05) in the high dose patients. Based on these findings, the authors concluded that using high dose rosuvastatin was associated with improved lipid-, inflammatory biomarkers and ventricular remodeling/myocardial fibrosis. This was not associated with adverse effects related to higher rosuvastatin dosage. The more potent therapeutic effects of high dose rosuvastatin after myocardial infarction would warrant its use in Chinese post AMI patients.

Luo R, Sun X, Shen F *et al.* Effects of High-Dose Rosuvastatin on Ventricular Remodelling and Cardiac Function in ST-Segment Elevation Myocardial Infarction. Drug design, development and therapy **2020; 14:3891-3898. http://www.ncbi.nlm.nih.gov/pubmed/?term=33061295**

Coronary plaque progression in statin treated patients – a review

Progression of atherosclerosis (AS) can be visualized by advanced imaging technology, enabling to optimize therapeutic strategies aimed at arresting progression or even regression of AS. This review article appraises risk factors that promote plaque progression despite statin therapy. The process of atherosclerosis is discussed as well as currently available imaging techniques allowing for detailed analysis of relevant plaque features; quantitatively and qualitatively. The risk for AS progression associated with LDL-c, Non-HDL-c, TC/HDL-C ratio, Lp(a), remnant cholesterol, and triglycerides is presented based on clinical trials analyzed changes in these lipids and lipoproteins and their effects on AS progression/regression. Lipoprotein variability (visit to visit) and non-lipid risk factors (blood pressure, hsCRP, diabetes, and chronic kidney disease) are discussed as well. The authors close off by underlining the importance of AS plaque as a predictor of future ASCVD events. To improve outcomes, a better understanding of the pathobiological processes would allow targeted treatment of mechanisms that promote AS progression.

Clark Iii D, Puri R, Nissen SE. Coronary Atherosclerotic Plaque Progression: Contributing Factors in Statin-Treated Patients. Expert Rev Cardiovasc Ther **2020. http://www.ncbi.nlm.nih.gov/pubmed/?term=33048622**

Mendelian randomization study predicts that cancer is less likely in statin treated patients

Statins and cancer are a sensitive and controversial topic based on observational evidence and the contradictory outcomes reported. This Mendelian randomization strategy to explore the harms or benefits of statins on cancer provides a new angle to address patients' and doctors' fears or expectations. Using data collected in the UK biobank (N=367 703) and focusing on 22-site specific cancer sites, variants in the HMG-CoA reductase gene, as a proxy for statin effects were analysed in 75 037 individuals that developed cancer. One standard deviation decrease in LDL-c was associated with a 24% lower risk of cancer; OR:0.76 (o.65-0.88; p=0.0003). However, when other genes, and variants in those genes (PCSK9, LDLr, NPC1L1, Apo C3, and LPL), were queried no protective effects were noted; OR: 1.10 (0.98-1.05; p=0.50). Based on their findings in the UK Biobank study, the authors suggest that statins are likely to reduce the risk of cancer but that these cancer protective effects are not related to their LDL-c lowering qualities butother so-called pleiotropic effects triggered by HMG-CoA inhibition.

Carter P, Vithayathil M, Kar S *et al.* **Predicting the effect of statins on cancer risk using genetic variants from a Mendelian randomization study in the UK Biobank.** eLife 2020; 9. http://www.ncbi.nlm.nih.gov/pubmed/?term=33046214

HEART UK consensus statement on Lipid lowering drugs in COVID-19 patients

The COVID-19 pandemic continues to create serious havoc in hospitalized patients that are infected with the SARS-CoV2 virus. The most important risk factors associated with complications and death are advanced age, obesity, hypertension, diabetes, and manifest cardiovascular disease. A significant proportion of these high COVID-19 risk patients are also diagnosed as having a high ASCVD risk. Lipid-lowering drugs, and most prominently statins, are used by many of those patients, and suggestions have been made that these medications could exacerbate COVID-19 related complications. This statement of the HEART UK addresses the questions raised regarding the continuation of lipid-lowering therapy in COVID-19 patients; based on current knowledge and strength of evidence. The Consensus view presented in this paper finds no evidence of harm to continue the prescription and use lipid-lowering agents in patients that have been using them to reduce their ASCVD risk. They recommend that lipid-lowering therapy be continued but warn for potential interactions with drugs used to treat COIVID-19; this is even more relevant in those who present with abnormal transaminases.

Iqbal Z, Ho JH, Adam S *et al.* **Managing hyperlipidaemia in patients with COVID-19 and during its pandemic: An expert panel position statement from HEART UK.** Atherosclerosis 2020; 313:126-136. http://www.ncbi.nlm.nih.gov/pubmed/?term=33045618

Relevant publications

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Basic Science publications

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