





A CURATED WEEKLY UPDATE OF ALL STATIN PUBLICATIONS

Update - Week 31, 2021



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

Managing lipids during pregnancy and breastfeeding

Pregnancy and ASCVD seems contradictory, women of childbearing age are no suspected to be at risk for CV complication during their pregnancy or when giving birth. For young women with Familial Hypercholesterolemia the situation is quite different. Reports of young women with a history of ASCVD complications before they became pregnant. In those with homozygous or with severe heterozygous FH this risk should evaluated and managed. This concise review shares current understanding on the effects of dyslipidemia in pregnancy and the risk associated with very high levels of plasma LDL-cholesterol. Managing lipids during pregnancy and breastfeeding is discussed and suggestions are based on the latestes American lipid management guidelines. The authors emphasise the importance of cross-collaboration between cardiologists, lipidologists and gynaecologists/obstetricians to address the complex care of women during this vulnerable period.

Thobani A, Hassen L, Mehta LS, Agarwala A. Management of Hypercholesterolemia in Pregnant Women with Atherosclerotic Cardiovascular Disease. <u>Curr Atheroscler</u>

Rep 2021; 23:58. http://www.ncbi.nlm.nih.gov/pubmed/?term=34345940

Comparing atorvastatin vs. rosuvastatin in post ACS patients

Atorvastatin and rosuvastatin are both high intensity statins with comparable LDL-c lowering efficacy in the high dosage ranges. Very few studies have compared the two high intensity statins, one RCT (the SATURN trial) showed very similar imaging outcomes. In this retrospective observational study in Qatari ACS patients, rosuvastatin was compared to atorvastatin, 1- and 12-months after hospital discharge. The primary endpoint, a composite of CVD-associated death, non-fatal ACS, and non-fatal stroke, was observed with similar frequencies in both groups; 1.3% vs 1% with an aHR: .64 (0.55-4.94; p=0.379) after 1 month and 4.8% vs 3.5%, with an aHR:1.48 (0.82-2.67, p+0.199) after 12 months. Safety paramaters were comparable in both groups with no statistically significant differences. Based on their findings the authors concluded that both atorvastatin and rosuvastatin had comparable safety and efficacy outcomes in post ACS patients.

Rahhal A, Khir F, Orabi B *et al.* A Comparative Study of High-intensity Rosuvastatin Versus Atorvastatin Therapy Post-acute Coronary Syndrome Using Real-world Data. <u>Curr Probl Cardiol 2021:100956.</u> http://www.ncbi.nlm.nih.gov/pubmed/?term=34363847

CHD free elderly (>70yrs) carry genetic variants associated with life-long lower LDL-c

Genetic variants associated with life-long lower plasma LDL c reductions can profoundly impact the development of ASCVD complications. In this study, PCSK9 and Apo B genetic variants were analyzed in patients >70years of age with no history of CHD events. Targeted sequencing was done in the 13 131 participants of the ASPirin in Reducing Events in the Elderly trial. 22 different loss of function variants in the PCSK9 and Apo B genes were discovered in 104 participants (1:126 patients). IN patients that carried the rare variants LDL-c was 19.4 mg (14.6%) lower compared to the non-carriers. This was adjusted for statin use. Statins were used by 16% of the carriers vs. 35% of the patients that did not carry the loss of function genetic variants. The PCSK9 R4SL variant was the most frequently observed, and patients with this genotype had on average a 15.5 mg (11.8%) Lower LDL-c in heterozygotes and 25.2 mg/dL (19.2%) in homozygotes (p<0.001). These findings suggest that genetic variants associated with lower plasma LDL-c are more frequently observed in CHD-free elderly individuals and confirm the by Mendelian

randomizations studies suggested protective effects of lifelong lower LDL-c on CHD outcomes.

Lacaze P, Riaz M, Sebra R *et al.* Protective lipid-lowering variants in healthy older individuals without coronary heart disease. <u>Open heart 2021</u>; 8. http://www.ncbi.nlm.nih.gov/pubmed/?term=34341098

Updated meta-analysis of statins use in COVID-19 patients

In this updated meta-analysis and systematic review, the authors examine the effects of statins in clinical outcomes in patients infected with the SARS-CoV-2 virus. All major electronic databases (PubMed, Google Scholar, Scopus, and preprint servers) were queried up to June 3rd, 2021. The primary endpoints used for this meta-analysis were allcause mortality and a composite endpoint of serious COVID-19 related complications. Included in the final analysis were 35 studies; 32 reported the outcome of all-cause mortality, and 15 reported the composite endpoint of severe COVID-19 illness. Statin use was associated with a significantly reduced risk of dying, HR: 0.70 (0.58-0.84), n= 21 127 and OR:0.63 (0.51-0.79) n=155 097. Serious COVID-19 related complications were observed less frequently in patients using statins vs. patients who were not on statins. OR: 0.80 (0.73-0.88) n=10 081. The authors suggested that their new findings do warrant large well designed clinical trials to investigate the benefits of statins in COVID-19 patients in order to provide the much-needed evidence that could prompt statins to be recommended for the prevention of life-threatening CoV-SARS-2 related complications. Kow CS, Hasan SS. The Association Between the Use of Statins and Clinical Outcomes in Patients with COVID-19: A Systematic Review and Meta-analysis. Am J Cardiovasc **Drugs 2021:1-15.** http://www.ncbi.nlm.nih.gov/pubmed/?term=34341972

Predictors of long term clinical outcomes in Hong Kong ischemic stroke patients

Family physicians play a leading role in the secondary prevention of stroke. In this retrospective, study data were collected in two major Hong Kong general outpatient clinics. Patients with a history of ischemic stroke (IS) and ≥2 outpatient visits during the recruitment period (1/1 -30/6 2010) were included and followed frequently until 31/12/2018. The primary outcome was a IS, TIA, or hemorrhagic stroke recurrence. The secondary outcomes were mortality and coronary artery disease (CAD). Included were 466 patients (mean age, 71.5 years). Over a median follow-up period of 8.7 years, 158 patients (33.9%) died. Eighty patients (17.2%) had a recurrent stroke, and 57 (12.2%) patients developed CAD. Age was an independent risk factor for recurrences and death. Statin use at

baseline was associated with a significant reduction of recurrent stroke, HR:0.476 (0.285-0.796; P=0.005. After adjusting for death as a competing risk factor, all-cause mortality risk was significantly lower in statin users, HR=0.61 (0.486-0.968, P=0.043). Other important predictors of survival were female sex, antiplatelet use, and higher diastolic blood pressure at baseline.

Han J, Choi YK, Leung WK *et al.* Long term clinical outcomes of patients with ischemic stroke in primary care - a 9-year retrospective study. <u>BMC family practice</u> 2021; 22:164. http://www.ncbi.nlm.nih.gov/pubmed/?term=34364364

Relevant publications

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- Yuan Y, Wang W, Shang X et al. Association between statin use and the risks of glaucoma in Australia: a 10-year cohort study. <u>Br J Ophthalmol</u> 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=34348924
- Yee J, Kim H, Heo Y et al. Association between CYP3A5 Polymorphism and Statin-Induced Adverse Events: A Systemic Review and Meta-Analysis. <u>Journal of personalized medicine</u> 2021; 11. http://www.ncbi.nlm.nih.gov/pubmed/?term=34357144
- Torri F, Ali G, Chico L et al. Anti-HMGCR antibodies and asymptomatic hyperCKemia. A case report. <u>Acta myologica: myopathies and</u> cardiomyopathies: official journal of the Mediterranean Society of Myology 2021; 40:105-108. http://www.ncbi.nlm.nih.gov/pubmed/?term=34355128
- Sommariva E, Stadiotti I, Casella M et al. Oxidized LDL-dependent pathway as new pathogenic trigger in arrhythmogenic cardiomyopathy. <u>EMBO molecular</u> <u>medicine</u> 2021; 13:e14365. http://www.ncbi.nlm.nih.gov/pubmed/?term=34337880
- Murdock DR, Venner E, Muzny DM et al. Genetic testing in ambulatory cardiology clinics reveals high rate of findings with clinical management implications. Genetics in medicine: official journal of the American College of Medical Genetics 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=34363016
- Liu Q, Dong T, Xi M et al. Tongxinluo Capsule Combined with Atorvastatin for Coronary Heart Disease: A Systematic Review and Meta-Analysis. <u>Evidence-based complementary and alternative medicine: eCAM</u> 2021; 2021:9413704. http://www.ncbi.nlm.nih.gov/pubmed/?term=34335841

- Leiherer A, Mündlein A, Brandtner EM et al. Lipid profiles of patients with manifest coronary versus peripheral atherosclerosis - is there a difference? <u>Journal of internal medicine</u> 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=34337800
- Klassen A, Faccio AT, Picossi CRC et al. Evaluation of two highly effective lipidlowering therapies in subjects with acute myocardial infarction. <u>Scientific</u> <u>reports</u> 2021; 11:15973. http://www.ncbi.nlm.nih.gov/pubmed/?term=34354179
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- Dounousi E, Tellis C, Pavlakou P et al. Association between PCSK9 Levels and Markers of Inflammation, Oxidative Stress, and Endothelial Dysfunction in a Population of Nondialysis Chronic Kidney Disease Patients. <u>Oxidative medicine</u> and cellular longevity 2021; 2021:6677012. http://www.ncbi.nlm.nih.gov/pubmed/?term=34336112
- 14. Chun KH, Park JM, Lee CJ *et al.* Statin Therapy in HIGH-Risk Individuals with NORMal Coronary Arteries: The HIGH-NORM Study. <u>J Atheroscler Thromb</u> 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=34334544
- Cartier LJ, Robin A, St-Cœur S et al. Impact of the 2016 Canadian Lipid Guidelines on Daily Practice at a Community Hospital. <u>Canadian journal of</u> <u>diabetes</u> 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=34340938
- Bellos I, Pergialiotis V, Perrea DN. Comparative efficacy of fixed-dose statin and antihypertensive agent combinations: A network meta-analysis of randomized controlled trials. <u>Vascul Pharmacol</u> 2021:106900. http://www.ncbi.nlm.nih.gov/pubmed/?term=34343694
- Ashraf AP, Sunil B, Bamba V et al. Case Studies in Pediatric Lipid Disorders and Their Management. <u>J Clin Endocrinol Metab</u> 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=34363474
- Yuan J, Li Y, Liu X et al. Atorvastatin Plus Low-Dose Dexamethasone May Be Effective for Leukemia-Related Chronic Subdural Hematoma but Not for Leukemia Encephalopathy: A Report of Three Cases. <u>Frontiers in oncology</u> 2021; 11:628927. http://www.ncbi.nlm.nih.gov/pubmed/?term=34336644
- 19. Villoz F, Lyko C, Del Giovane C *et al.* Tolerability of statin-based management of patients with a history of statin-associated muscle symptoms: protocol for a

- systematic review. <u>BMJ Open 2021</u>; 11:e052341. http://www.ncbi.nlm.nih.gov/pubmed/?term=34344686
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- 22. Paul M, Paul P, Dey D *et al.* A Case of Statin-Associated Immune-Mediated Necrotizing Myopathy, Successfully Treated With Intravenous Immunoglobulin. <u>Cureus</u> 2021; 13:e16001.
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- 24. Nowakowska MK, Lei X, Thompson MT *et al.* Association of statin use with clinical outcomes in patients with triple-negative breast cancer. <u>Cancer 2021</u>. http://www.ncbi.nlm.nih.gov/pubmed/?term=34342892
- 25. Majd Z, Mohan A, Abughosh SM. Using group-based trajectory modeling to characterize the association of past ACEIs/ARBs adherence with subsequent statin adherence patterns among new statin users. <u>Journal of the American</u> <u>Pharmacists Association: JAPhA</u> 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=34344613
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- Jeong SH, Lee HS, Chung SJ et al. Effects of statins on dopamine loss and prognosis in Parkinson's disease. <u>Brain</u> 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=34347020
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- Choi WG, Baek MJ, Rha SW et al. Impact of initial very low-level low-density lipoprotein cholesterol on the prognosis of acute myocardial infarction patients. Coronary artery disease 2021.
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Basic Science publications

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- Song S, Niu M, Liang Q et al. Statin Treatment Induced a Lipogenic Expression Hierarchical Network Centered by SREBF2 in the Liver. <u>Frontiers in</u> <u>endocrinology</u> 2021; 12:573824. http://www.ncbi.nlm.nih.gov/pubmed/?term=34349727
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