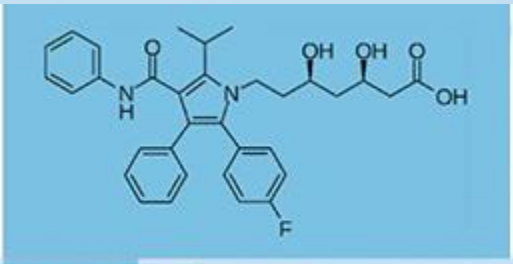
IAS STATIN NEWSLETTER



INTERNATIONAL ATHEROSCLEROSIS SOCIETY

A CURATED WEEKLY UPDATE OF ALL STATIN PUBLICATIONS

Update - Week 27, 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

Comparing atorva 40 mg with atorva 10 mg + Ezetimibe 10 mg

combination of atorvastatin 10 mg + ezetimibe 10 mg. Near-infrared spectroscopy-intravascular ultrasonography was used at baseline and after 12 months follow-up to determine differences in percent atheroma lesions (PAV) in intermediate lesion segments. Both groups showed significant reductions of LDL-c of 40% and 38%, respectively, and no statistically significant mean differences between the two groups. Absolut change in PAV was -3.2% in the patients allocated to atorvastatin 40 mg vs. -2.9% in those taking 10 mg atorvastatin + 10 mg ezetimibe, resulting in a mean between-group difference of 0.5% (-2.4%

to 2.8%). The pre-defined non-inferiority margin of 5% was not exceeded. The lipid core burden did not change; no difference between the two groups were observed. The authors concluded that both treatment regimens showed similar outcomes in LDL-c reductions and coronary atherosclerosis regression.

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. Am J Cardiol 2021; 154:22-28. http://www.ncbi.nlm.nih.gov/pubmed/?term=34238445

Reduced mortality associated with statin use in hospitalized diabetic COVID-19 patients

Statins seem an attractive option for reducing COVID-19 complications and mortality. Currently, most studies that examined the effects of statins are observational, retrospective studies. In this single US hospital retrospective evaluation, 922 patients were evaluated for statin use and a diagnosis of DM2. Using a 1:1 propensity score matching plus multivariate regression analysis, 250 patients (27.1%) that used statins and 136 diabetic patients (32.9%) on statins were compared to those not using statins. Overall statin use was associated with reduced mortality, OR: 0.61 (0.42-0.90; p=0.01). The subgroup analysis of diabetic patients showed an even more substantial impact of statin use, OR:0.35 (0.21-0.61, p<0.001). In contrast with non-diabetic patients that used statins and in whom no significant difference was noted, OR: 1.21 (0.67-2.17; p=0.52). These findings align with earlier observational studies that examined the impact of statins on COID-19 related morbidity and mortality and emphasized the importance of conducting RCTs to address this important dilemma.

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. http://www.ncbi.nlm.nih.gov/pubmed/?term=34246277

PC-AKI risk reduced in Chinese patients using pre-admission statins

A recurring theme in statin publications is the protective effects of statin in post-contrast acute kidney injury (PC-AKI). In this prospective observational study, 4386 Chinese patients had a CAG or PCI procedure between 2006 and 2019 in a single consortium of hospitals. PC-AKI was observed in 17.9% of the patients; pre-operative statins were used by 83.8%. Using multivariate regression analysis, the risk of PC-AKI was significantly reduced in patients that used stating prior to their hospitalization. OR: 0.5757 (p<0.001). similar outcomes were noted for patients using atorvastatin or rosuvastatin. OR: 1.052 (P=0.558). In subsequent analysis, a direct protective effect of statin was noted that was not correlated with LDL-c lowering (P=0.277) or hsCRP reduction (anti-inflammatory effects (p=0.596)]. Although LDL-

c lowering and hsCRP reductions had a mediating effect, this was calculated to contribute no more than 1% of the observed benefits. The authors suggested that the pre-operative use of statins is an independent protective factor for PC-AKI. This was independent of the type of statins used and seemed to be a direct effect not related to LDL-c or hsCRP lowering properties.

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

Guideline recommended treatment of FH patient needs to be improved

The introduction of new potent non-statin LDL-c lowering drugs has prompted recently released lipid management guidelines to focus on improved cholesterol control in Familial hypercholesterolemia (FH). The impact on real-life clinical management of FH patients remains poor, as illustrated by this report from the (GOAL) Guidelines Oriented Approach to Lipid Lowering, Canada project. Physicians were invited to participate, and 248/750 agreed to enroll 12 consecutive patients with CVD or FH and an LDL-c >2.0 mmol/L, despite maximally tolerated statin therapy. The patient had 2 follow-up visits 4-6 months apart. Physicians received online reminders of the Canadian 2009 treatment recommendations. Among the 2009 enrolled patients, there were 1054 (52.4%) patients with CVD only, 636 (31.7%) with FH only, and 319 (15.9%) with both CVD and FH. FH patients were younger, more likely to be female, non-white, and had significantly higher baseline LDL-c than CVD-only patients, 3.92±1.48 versus 2.96±0.94, P<0.0001, respectively. Statins were less frequently prescribed to FH patients (70.6% versus 79.2%, P=0.0001); however, ezetimibe use was used more by FH patients (28.1% versus 20.4%, P=0.0003). Guideline recommended LDL-c targets (≥ 50% reduction from pre-treatment level or low-density lipoprotein <2.5 mmol/L) was noted in 45.3% at baseline in FH only patients. This increased to 65.8% and 73.6% by visits 2 and 3. None of the CVD patients were at recommended level (≤2.0 mmol/L) at baseline. This increased to 44.3% and 53.3% on the second and third visits. When comparing baseline and last available follow-up visit, 22.0% of patients with FH only, 45.8% of those with CVD only (P<0.0001), and 55.2% with both FH+CVD (P<0.0001) achieved guideline LDL-c goals. The authors concluded that they observed significant treatment inertia in the management of FH patients and suggested intensified educational and support activities to improve the implementation of guideline recommendations.

Langer A, Mancini GBJ, Tan M *et al.* Treatment Inertia in Patients With Familial Hypercholesterolemia. J Am Heart Assoc 2021; 10:e020126.
http://www.ncbi.nlm.nih.gov/pubmed/?term=34238023

Meta-analysis evaluating statins effect on atherosclerosis in Chinese patients

This meta-analysis examined the effect of statins on coronary atherosclerosis. In total, 12 studies that enrolled 1180 Chinese patients were included for the final analysis. When comparing statin use with controls, the plaque area was reduced, mean difference of -1.21 (-2.03 to -.038). Changes in total C, TG, and LDL-c were lower in the statin-treated patients as well. The effective clinical score showed better results as well, mean difference of 3.64 (1.39-9.53, p=0.008). No significant changes were observed for carotid intima-media thickness, mean difference =−0.41 (−0.88 to −0.06; Z =1.7; P=0.09), hsCRP, mean difference =−1.61(−3.59 to 0.37; Z =1.7; P=0.09) and HDL-c, mean difference =0.14 (−0.02 to 0.30; Z =2.54; P=0.09).

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. http://www.ncbi.nlm.nih.gov/pubmed/?term=34237978

Relevant publications

1. **Shabani M, Bakhshi H, Ostovaneh MR *et al.* Temporal change in inflammatory biomarkers and risk of cardiovascular events: the Multi-ethnic Study of Atherosclerosis. ESC heart failure 2021.** http://www.ncbi.nlm.nih.gov/pubmed/?term=34240828
2. **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.** http://www.ncbi.nlm.nih.gov/pubmed/?term=34225103
3. **Rhainds D, Brodeur MR, Tardif JC. Lipoprotein (a): When to Measure and How to Treat? Curr Atheroscler Rep 2021; 23:51.** http://www.ncbi.nlm.nih.gov/pubmed/?term=34235598
4. **Plakogiannis R, Sorbera M, Fischetti B, Chen M. The Role of Antisense Therapies Targeting Lipoprotein(a). Journal of cardiovascular pharmacology 2021; 78:e5-e11.** http://www.ncbi.nlm.nih.gov/pubmed/?term=34232223
5. **Kollias A, Kyriakoulis KG, Kyriakoulis IG *et al.* Statin use and mortality in COVID-19 patients: Updated systematic review and meta-analysis. Atherosclerosis 2021; 330:114-121.** http://www.ncbi.nlm.nih.gov/pubmed/?term=34243953

6. Jayatilaka S, Desai K, Rijal S, Zimmerman D. Statin-Induced Autoimmune Necrotizing Myopathy. J Prim Care Community Health 2021; 12:21501327211028714. http://www.ncbi.nlm.nih.gov/pubmed/?term=34219515
7. 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. Curr Atheroscler Rep 2021; 23:50. http://www.ncbi.nlm.nih.gov/pubmed/?term=34226979
8. Bohara S, Gaonkar VB, Garg K *et al.* Effect of statins on functional outcome and mortality following aneurysmal subarachnoid hemorrhage - Results of a meta-analysis, metaregression and trial sequential analysis. Clin Neurol Neurosurg 2021; 207:106787. http://www.ncbi.nlm.nih.gov/pubmed/?term=34225002
9. Afifi T, Obeid M, Abdelati M *et al.* WHO/International Society of Hypertension risk prediction charts versus the UK Prospective Diabetes Study risk engine for cardiovascular risk assessment among patients with type 2 diabetes: a comparative study. Lancet 2021; 398 Suppl 1:S3. http://www.ncbi.nlm.nih.gov/pubmed/?term=34227962
10. Yayan J, Bald M, Franke KJ. No Independent Influence of Statins on the Chronic Obstructive Pulmonary Disease Exacerbation Rate: A Cohort Observation Study Over 10 Years. International journal of general medicine 2021; 14:2883-2892. http://www.ncbi.nlm.nih.gov/pubmed/?term=34234518
11. Sutton SS, Magagnoli JC, Cummings TH, Hardin JW. Statin Exposure and Risk of Prosthetic Joint Infection After Total Knee or Hip Arthroplasty Among U.S. Veterans. The Journal of arthroplasty 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=34229942
12. Seppala LJ, van de Loo B, Schut M *et al.* A Propensity Score Matched Approach to Assess the Associations of Commonly Prescribed Medications with Fall Risk in a Large Harmonized Cohort of Older Ambulatory Persons. Drugs Aging 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=34224104
13. Santos Junior GGD, Araújo PSR, Leite KME *et al.* The Effect of Atorvastatin + Aspirin on the Endothelial Function Differs with Age in Patients with HIV: A Case-Control Study. Arquivos brasileiros de cardiologia 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=34231792
14. Saito K, Sato Y, Nakatani E *et al.* Statin exposure and pancreatic cancer incidence: A Japanese regional population-based cohort study, the Shizuoka Study. Cancer prevention research (Philadelphia, Pa.) 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=34244151
15. Mueller MC, Usadel S, Kern WV *et al.* Proportion of patients eligible for statin therapy substantially varies between different cardiovascular disease risk calculators and guidelines used. Int J STD AIDS 2021:9564624211029392. http://www.ncbi.nlm.nih.gov/pubmed/?term=34233537
16. Huang CT, Liang YJ. Anti-tumor effect of statin on pancreatic adenocarcinoma: From concept to precision medicine. World journal of clinical cases 2021; 9:4500-4505. http://www.ncbi.nlm.nih.gov/pubmed/?term=34222418
17. Harewood R, Disney R, Kinross J *et al.* Medication use and risk of proximal colon cancer: a systematic review of prospective studies with narrative synthesis and

meta-analysis. Cancer Causes Control 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=34224060
18. 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. http://www.ncbi.nlm.nih.gov/pubmed/?term=34242482
19. Choi J, Kim H, Jun J *et al.* Recurrent Pancreatitis in a Pregnant Woman with Severe Hypertriglyceridemia Successfully Managed by Multiple Plasmapheresis. J Atheroscler Thromb 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=34219115
20. Bertero E, Heusch G, Münzel T, Maack C. A pathophysiological compass to personalize antianginal drug treatment. Nat Rev Cardiol 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=34234310

Basic Science publications

1. Saadat S, Boskabady MH. Anti-inflammatory and Antioxidant Effects of Rosuvastatin on Asthmatic, Hyperlipidemic, and Asthmatic-Hyperlipidemic Rat Models. Inflammation 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=34226988
2. Liang W, Shi J, Xia H, Wei X. A Novel Ruthenium-Fluvastatin Complex Downregulates SNCG Expression to Modulate Breast Carcinoma Cell Proliferation and Apoptosis via Activating the PI3K/Akt/mTOR/VEGF/MMP9 Pathway. Oxidative medicine and cellular longevity 2021; 2021:5537737. http://www.ncbi.nlm.nih.gov/pubmed/?term=34221232
3. Guo G, Cai J. Rosuvastatin alleviated the liver ischemia reperfusion injury by activating the expression of peroxisome proliferator-activated receptor gamma (PPARγ). J Bioenerg Biomembr 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=34235609
4. Cheon YH, Lee CH, Kim S *et al.* Pitavastatin prevents ovariectomy-induced osteoporosis by regulating osteoclastic resorption and osteoblastic formation. Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie 2021; 139:111697. http://www.ncbi.nlm.nih.gov/pubmed/?term=34243614
5. Abo-Zalam HB, El-Denshary ES, Abdelsalam RM *et al.* Therapeutic advancement of simvastatin-loaded solid lipid nanoparticles (SV-SLNs) in treatment of hyperlipidemia and attenuating hepatotoxicity, myopathy and apoptosis:

Comprehensive study. Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie 2021; 139:111494.
http://www.ncbi.nlm.nih.gov/pubmed/?term=3424359

This activity is supported by an educational grant from Viatris.
© P.J. Lansberg