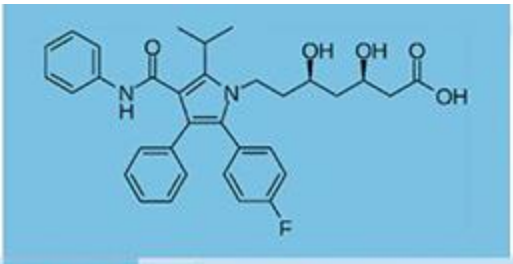
IAS STATIN NEWSLETTER



INTERNATIONAL ATHEROSCLEROSIS SOCIETY

A CURATED WEEKLY UPDATE OF ALL STATIN PUBLICATIONS

Update - Week 26, 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

Review on the use of omega 3-fatty acids to reduce ASCVD risk

Statins have spurred unprecedented reductions in ASCVD risk in primary and in secondary prevention settings. Despite these successes, residual risk remains a formidable challenge with potential, impressive gains in survival and morbidity. Triglycerides have surfaced not only as powerful predictors of residual CVD risk but have also become a therapeutic target. One class of lipid-lowering drugs, the omega-3 fatty acid/fish oils, has risen from obscurity and is now a powerful new asset in the residual risk battle. The authors provide a comprehensive overview of our current understanding and the conflicting evidence. Promising results from recent studies showed impressive reductions in CV complications that could not be explained by the mild TG reductions observed in the participating patients. Higher dosages and specific formulations are likely to play a pivotal role in the observed benefits. However, safety issues such as the increased risk for atrial fibrillation (AF) and hemorrhagic complications underline that omega 3-fatty acids have not been wholly embraced in daily clinical practice. The authors recommend using high dose omega 3-fatty acids, based on the formulations in the recent secondary prevention trials, in statin-treated hyper-triglyceridemic patients classified as high or very-high CVD risk.

Tadic M, Sala C, Grassi G *et al.* Omega-3 Fatty Acids and Coronary Artery Disease: More

Questions Than Answers. Journal of clinical medicine 2021; 10. http://www.ncbi.nlm.nih.gov/pubmed/?term=34200081

One third of low-risk individuals have sub-clinical atherosclerosis

Lipid-lowering guidelines recommend statins for patients at high or very high risk for ASCVD. The authors of this article evaluated Korean individuals considered low risk and their 5-year probability of developing CVD complications based on CTA imaging. Participants (N=3272) had a voluntary general health examination and lacked an indication for statins. A cardiac event was defined as a composite of cardiac death, nonfatal myocardial infarction, unstable angina requiring hospitalization, or late coronary revascularization Patients were classified as normal coronary arteries, non-obstructive coronary artery disease (CAD), with diameter stenosis <50% and obstructive CAD, diameter stenosis >50%. These changes were observed in 2338 (71%), 809 (24.7%), and 125 (3.8%), respectively. The calculated 6-year event-free survival year were 99.2% ±0.2% in subjects with normal coronary arteries, 98.2% ±0.6% in those with non-obstructive CAD, and 90.2% ±2.7% in those with obstructive CAD (log-rank p < 0.001). Predictors for subclinical obstructive CAD, based on multivariable regression analysis, were LDL-C, OR: 1.012 (1.005−1.019); HDL-C, OR: 0.968; (0.952−0.984); age OR: 1.080 (1.040−1.121) and male sex, OR: 3.102 (1.866−5.155); all p < 0.05. The authors suggested a stricter LDL-c control to improve primary prevention in a relatively low-risk population based on these findings. Park HW, Kim YG, Park GM *et al.* Cholesterol Control for Subclinical Coronary Atherosclerosis in Subjects Without Indication for Statin Therapy. Am J Cardiol 2021; 153:51-57. http://www.ncbi.nlm.nih.gov/pubmed/?term=34176598

Impact of optimal medical therapy on 10-year survival in post-CABG/PCI patients

This sub-analysis of the SYNTAXES (Synergy Between PCI With Taxus and Cardiac Surgery Extended Survival) study showed the impact of optimal medical therapy (OMT) on 10-year survival. OMT was defined as the combination of 4 types of medications: at least 1 antiplatelet drug, statin, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, and beta-blocker. OMT was stratified by the number of OMT medications used after 5-years and assess mortality after 5-years. Of the 1472 patients on OMT at 5-years, survival was significantly better compared to those on ≤ 2 types of medications; 13.1% vs. 19.9%; adjusted HR: 0.470 (0.292-0.757; P=0.002). No difference in mortality was noted between those on OMT and patients using 3 types of medication. Post-CABG patients using statins and antiplatelet medication at 5-years had lower 10-year mortality than those without. The authors concluded that patients with 3-vessel disease and or left-main disease that underwent PCI or CABG showed improved survival after 10-years follow-up if guideline-recommended OMT was used at 5-years.

Kawashima H, Serruys PW, Ono M *et al.* Impact of Optimal Medical Therapy on 10-Year Mortality After Coronary Revascularization. J Am Coll Cardiol 2021; 78:27-38. http://www.ncbi.nlm.nih.gov/pubmed/?term=34210411

The LDL-c/Apo B ratio predicts MACE in secondary prevention patients

Lipid management guidelines focus on LDL-c as a primary target for reducing ASCVD risk. Despite adequate LDL-c reduction, the risk for cardiac events remains high in those classified as high- or very-high ASCVD risk. This residual risk is partly captured by determining the qualitative properties of LDL particles, and LDL particle size is considered an important parameter. Each LDL carries a single apo B molecule, and the ratio of LDL-c/Apo B provides a reasonable estimate of LDL particle size. The impact of this ratio on ASCVD risk was estimated in 1678 patients with cardiovascular disease. Prospective MACE (cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke) were prospectively recorded over a 9.9 ±4.6 years period (>16,000 patient-years). The baseline LDL-C/ApoB ratio was 1.36 ± 0.28. In total, 558 first events were recorded during the follow-up period. Univariate Cox proportional hazard analysis showed an HR of 0.90 (0.82–0.98; p = 0.014). After adjustment for age, gender, the intensity of statin treatment, hypertension, history of smoking, type 2 diabetes, body mass index, and Apo B, an HR: 0.87 (0.78–0.97; p = 0.013) was observed. The authors concluded that the LDL-c/Apo B ratio was an independent predictor of subsequent MACE in patients with established CVD.

Drexel H, Larcher B, Mader A *et al.* The LDL-C/ApoB ratio predicts major cardiovascular events in patients with established atherosclerotic cardiovascular disease. Atherosclerosis 2021; 329:44-49. http://www.ncbi.nlm.nih.gov/pubmed/?term=34183170

Barriers to lipid lowering medication adherence in Jordanian dyslipidemic patients

Medication adherence remains the major barrier to minimize CVD risk in patients eligible for statin treatment. In this investigation of lipid-lowering drug adherence study, 228 dyslipidemic Jordanian patients were evaluated. They also shared their beliefs about medication by using the Beliefs about Medicines Questionnaire. The majority of patients (78%) were non-adherent. Ost important negative associations consisted of concerns of prescription drug use (B = -0.41, p-value < 0.01), duration of dyslipidaemia (B = -0.22, p-value < 0.01), and the number of medications (B = -0.64, p-value < 0.01). Predictors of improved adherence included the necessity of prescription drug use (B = 0.43, p-value < 0.01), taking statin and fibrate (B = 2.04, p-value < 0.01), and moderate-intensity statin (B = 2.34, p-value < 0.01). The most frequently cited belief for non-adherence was "My medicine to lower my cholesterol disrupted my life" (3.50 ±0.99). In this Jordanian dyslipidemic

population, adherence to lipid-lowering medication was very poor. Strategies addressing predictors of adherence and changing believes on medication use could help to overcome these barriers, improve adherence and reduce serious ASCVD outcomes.
Alefishat E, Jarab AS, Al-Qerem W, Abu-Zaytoun L. Factors Associated with Medication Non-Adherence in Patients with Dyslipidemia. Healthcare (Basel) 2021; 9. http://www.ncbi.nlm.nih.gov/pubmed/?term=34203226

Relevant publications

1. Zvizdić F, Begić E, Dilić M *et al.* Effect of atorvastatin on systolic and diastolic function in patients with heart failure with reduced ejection fraction (HFrEF). Medicinski glasnik : official publication of the Medical Association of Zenica-Doboj Canton, Bosnia and Herzegovina 2021; 18. http://www.ncbi.nlm.nih.gov/pubmed/?term=34212706
2. Zein A, Sulistiyana CS, Khasanah U *et al.* Statin and mortality in COVID-19: a systematic review and meta-analysis of pooled adjusted effect estimates from propensity-matched cohorts. Postgraduate medical journal 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=34193549
3. Yamamuro S, Shinozaki T, Iimuro S, Matsuyama Y. Mediational g-formula for time-varying treatment and repeated-measured multiple mediators: Application to atorvastatin's effect on cardiovascular disease via cholesterol lowering and anti-inflammatory actions in elderly type 2 diabetics. Stat Methods Med Res 2021:9622802211025988. http://www.ncbi.nlm.nih.gov/pubmed/?term=34187236
4. Xiong X, Wu Z, Qin X *et al.* Statins reduce mortality after abdominal aortic aneurysm repair: A systematic review and meta-analysis. Journal of vascular surgery 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=34197945
5. Whiteley WN, Gupta AK, Godec T *et al.* Long-Term Incidence of Stroke and Dementia in ASCOT. Stroke 2021:Strokeaha120033489. http://www.ncbi.nlm.nih.gov/pubmed/?term=34192893
6. Thiermeier N, Lämmer R, Mardin C, Hohberger B. Erlanger Glaucoma Registry: Effect of a Long-Term Therapy with Statins and Acetyl Salicylic Acid on Glaucoma Conversion and Progression. Biology (Basel) 2021; 10. http://www.ncbi.nlm.nih.gov/pubmed/?term=34208432
7. Rogula S, Błażejowska E, Gąsecka A *et al.* Inclisiran-Silencing the Cholesterol, Speaking up the Prognosis. Journal of clinical medicine 2021; 10. http://www.ncbi.nlm.nih.gov/pubmed/?term=34199468
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9. Patel D, Busch R. Omega-3 Fatty Acids and Cardiovascular Disease: A Narrative Review for Pharmacists. Journal of cardiovascular pharmacology and therapeutics 2021:10742484211023715. http://www.ncbi.nlm.nih.gov/pubmed/?term=34191622
10. Olszewska-Parasiewicz J, Szarpak Ł, Rogula S *et al.* Statins in COVID-19 Therapy. Life (Basel) 2021; 11. http://www.ncbi.nlm.nih.gov/pubmed/?term=34208435
11. Mesi O, Lin C, Ahmed H, Cho LS. Statin intolerance and new lipid-lowering treatments. Cleveland Clinic journal of medicine 2021; 88:381-387. http://www.ncbi.nlm.nih.gov/pubmed/?term=34210712
12. Mayo J, Hoffman T, Smith R, Kellicut D. Lipoprotein(a) as a unique primary risk factor for early atherosclerotic peripheral arterial disease. BMJ case reports 2021; 14. http://www.ncbi.nlm.nih.gov/pubmed/?term=34193454
13. Lee MC, Peng TR, Chen BL *et al.* Effects of various statins on depressive symptoms: A network meta-analysis. Journal of affective disorders 2021; 293:205-213. http://www.ncbi.nlm.nih.gov/pubmed/?term=34217957
14. Hasan S, Naugler C, Decker J *et al.* Laboratory reporting of framingham risk score increases statin prescriptions in at-risk patients. Clin Biochem 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=34197811
15. Gouda P, Savu A, Bainey KR *et al.* Long-term risk of death and recurrent cardiovascular events following acute coronary syndromes. PLoS One 2021; 16:e0254008. http://www.ncbi.nlm.nih.gov/pubmed/?term=34197547
16. Formanowicz D, Krawczyk JB, Perek B *et al.* Management of High-Risk Atherosclerotic Patients by Statins May Be Supported by Logistic Model of Intima-Media Thickening. Journal of clinical medicine 2021; 10. http://www.ncbi.nlm.nih.gov/pubmed/?term=34209480
17. Erkol A, Dalgıç Y, Yıldırım S, Turan B. Incidence and predictors of prolonged hemodynamic depression after carotid artery stenting: Yet another benefit of statins? Clin Neurol Neurosurg 2021; 207:106786. http://www.ncbi.nlm.nih.gov/pubmed/?term=34198224
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22. Watanabe LM, Navarro AM, Seale LA. Intersection between Obesity, Dietary Selenium, and Statin Therapy in Brazil. Nutrients 2021; 13. http://www.ncbi.nlm.nih.gov/pubmed/?term=34204631

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27. Jurcau A, Simion A. Cognition, Statins, and Cholesterol in Elderly Ischemic Stroke Patients: A Neurologist's Perspective. Medicina (Kaunas, Lithuania) 2021; 57. http://www.ncbi.nlm.nih.gov/pubmed/?term=34199243
28. Eastwood SV, Mathur R, Sattar N *et al.* Ethnic differences in guideline-indicated statin initiation for people with type 2 diabetes in UK primary care, 2006-2019: A cohort study. PLoS Med 2021; 18:e1003672. http://www.ncbi.nlm.nih.gov/pubmed/?term=34185782
29. Cicero AFG, Fogacci F, Cincione I. Evaluating pharmacokinetics of bempedoic acid in the treatment of hypercholesterolemia. Expert Opin Drug Metab Toxicol 2021:1-7. http://www.ncbi.nlm.nih.gov/pubmed/?term=34197267
30. Božina N, Ganoci L, Simičević L *et al.* Drug-drug-gene interactions as mediators of adverse drug reactions to diclofenac and statins: a case report and literature review. Arhiv za higijenu rada i toksikologiju 2021; 72:114-128. http://www.ncbi.nlm.nih.gov/pubmed/?term=34187111

Basic Science publications

1. Tomaszewski M, Zolkowska D, Plewa Z *et al.* Effect of acute and chronic exposure to lovastatin on the anticonvulsant action of classical antiepileptic drugs in the mouse maximal electroshock-induced seizure model. Eur J Pharmacol 2021; 907:174290. http://www.ncbi.nlm.nih.gov/pubmed/?term=34217711
2. Sun T, Xing HL, Chen ZZ *et al.* Simvastatin reverses the harmful effects of high fat diet on titanium rod osseointegration in ovariectomized rats. J Bone Miner Metab 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=34189660
3. Sivasinprasasn S, Wikan N, Tocharus J *et al.* Pelargonic acid vanillylamide and rosuvastatin protect against oxidized low-density lipoprotein-induced endothelial dysfunction by inhibiting the NF-κB/NLRP3 pathway and improving cell-cell

junctions. Chemico-biological interactions 2021; 345:109572. http://www.ncbi.nlm.nih.gov/pubmed/?term=34217687
4. Rimpelová S, Kolář M, Strnad H *et al.* Comparison of Transcriptomic Profiles of MiaPaCa-2 Pancreatic Cancer Cells Treated with Different Statins. Molecules (Basel, Switzerland) 2021; 26. http://www.ncbi.nlm.nih.gov/pubmed/?term=34207840
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