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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

Does it matter how you lower LDL-?

To reduce atherosclerotic cardiovascular complications lowering LDL-c is first and foremost, but does it matter which drug to use? In this single case of an elderly Japanese woman with repeated in-stent restenosis (ISR), it seemed that it did. After her primary PCI, she had two subsequent PCI for ISR. Her medication was up-titrated to rosuvastatin 5 mg + evolocumab 420 mg (1 x per month). With this regimen, her LDL-c was reduced to 10 mg/dL and hs-CRP 0.24 mg/dL. Despite the very low LDL-c, she had a third episode of ISR. After other potential causes for ISR, e.g., metal allergies, were excluded, her rosuvastatin was up-titrated to 20 mg (maximum dosage in Japan). Her LDL-c remained the same, 10 mg/dL, but her hs-CRP was further reduced to 0.09 mg/dL. Although this is only a single case, the findings suggest that a maximal dose of statins could be pivotal for secondary prevention. The absence of recurrences suggests that the maximum statin dosage should not be discarded when alternative and powerful LDL-c lowering interventions are used.

Yonezawa Y, Sakuma M, Abe S *et al.* Repeated In-Stent Restenosis Despite Aggressive Lipid Lowering by PCSK-9 Inhibitor Treatment: A Case Report. [Tohoku J Exp Med 2021; 255:123-](#)

126. <http://www.ncbi.nlm.nih.gov/pubmed/?term=34645737>

Shin J, Kim H, Yim HW *et al.* Angiotensin-converting enzyme inhibitors versus

In patients with statin related NODM which blood pressure lowering drug is better?

New onset diabetes (NODM) is a well-recognized adverse effect of high dose high-intensity statins. Not only the statin but the patients' health status is at least as relevant to predict and prevent and manage NODM. In this retrospective study, based on patient data collected between 2009 and 2012 in two large hospitals in Seoul, South Korea, the impact of ACEi and ARBs in combination with statins was evaluated over a follow-up period of 5 years. Of the 11 703 patients, 24.9% (N=2916) took ACEi and 75.1% (N=9189) used ARBs. The risk of developing diabetes was significantly lower in patients using ACEi, HR:0.13 ($p<0.001$) combined with statins or without statins, HR:0.15 ($P=0.009$), compared to patients using ARBs. Additional risk factors for NODM in patients using statins were Age ≥ 60 years, HR=1.49 ($P=0.010$); BMI ≥ 25 , HR=1.96 ($P<0.010$); use of calcium channel blockers, HR=1.47 ($P=.010$), and diuretics, HR=1.48 ($P=0.010$). From the results of NODM compared to ARBs, irrespective of statin use. The observational design of this study warrants properly designed clinical trials to confirm these important findings.

angiotensin receptor blockers: New-onset diabetes mellitus stratified by statin use. Journal of clinical pharmacy and therapeutics 2021.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=34668200>

Statins in hemodialysis, some patients do benefit.

Two large clinical endpoint trials failed to show the benefits of statins in hemodialysis patients. Since these landmark publications, several studies showed potential protective effects of statins in specific subgroups of hemodialysis patients. In this prospective multi-center study, 234 consecutive hemodialysis patients were followed for a period of 3-years, or until an occurrence of a MACE (a composite of all-cause death and non-fatal myocardial infarction). A MACE occurred in 55 patients, and those that were not using statins had a significantly increased risk ($P<0.001$). A Cox multivariable proportional risk analysis showed an HR of 0.30 (0.11-0.81) for a MACE in statin users. A set of clinical factors were associated with statin benefits; male, elderly, lower body mass index, lower abdominal circumference, hypertension, diabetes, higher C-reactive protein, symptomatic heart failure, lower left ventricular function, non-acute coronary syndrome, and shorter stent length. Despite the neutral outcomes in earlier trials, statins seem to provide cardiovascular benefits in subgroups of hemodialysis patients. Certain clinical characteristics amplified the observed secondary prevention benefits of statins. Horikoshi T, Nakamura T, Yoshizaki T *et al.* Stratification Analysis of Statin Effect on Major Adverse Cardiac Events after Percutaneous

Coronary Intervention in Patients on Hemodialysis. Journal of cardiovascular pharmacology 2021. <http://www.ncbi.nlm.nih.gov/pubmed/?term=34654788>

The harms and benefits of statins in stroke patients that had an IV thrombolysis

This systematic review and meta-analysis explored the safety and efficacy of statins, before admission and during a hospital stay, in patients that received intravenous thrombolysis (IVT) for an acute ischemic stroke (AIS). Twenty-two observational studies (N=17 554) were included in the meta-analysis. Patients that used statins prior to their AIS were more likely to suffer an intracranial hemorrhage (ICH); symptomatic ICH, OR=1.31 (1.07-1.59, P=0.008); any ICS, OR=1.21 (1.03-1.43, P=0.02). Pre-admission statin use showed no association with 3-month mortality, 3-month favorable functional outcome (FFO, modified Rankin Scale (mRS) score 0–1), and 3-month functional independence (FI; mRS score 0–2). Patients that used statins during their hospital stay had a reduced risk for ICH, OR=0.46 (0.21–1.00, p = 0.045); any ICH, OR=0.51 (0.27–0.98; p = 0.04); 3-month mortality, OR=0.42 (0.29–0.62; p < 0.001); an increased probability of 3-month FFO (OR 1.33; 95% CI 1.02–1.744; p = 0.04), and 3-month FI, OR=1.41 (1.11–1.80; p = 0.005). Based on these observational findings, in-hospital use of statins may not only be safe but could have a favorable effect on clinical outcomes as well.

Guo Y, Guo X, Zhao K *et al.* Statin Use and Outcomes of Patients With Acute Ischemic Stroke Treated With Intravenous Thrombolysis: A Systematic Review and Meta-Analysis. Frontiers in neurology 2021; 12:734927. <http://www.ncbi.nlm.nih.gov/pubmed/?term=34630305>

Time to switch from LDL-c to Apo B

This extensive review, including a rich list of 278 literature refs, provides answers to all relevant questions regarding apo B. Basic metabolism and the prominent role of apo B for CV risk evaluation compared to LDL-c measurements or estimations. In patients with triglyceride elevations, LDL-c levels underestimate the atherogenic potential of apo B carrying lipoproteins, and apo B is a far better predictor because a single protein is found on every atherogenic particle. In contrast, simple LDL-c levels are unable to reflect particle numbers. Standardization of apo B measurement and prices have improved significantly and more robust compared to LDL-c measurements. What makes apo B attractive for patients is that there is no need for fasting before the blood draw, a rule needed to ensure accuracy for an accurate estimate based on the Friedewald formula. The authors introduce mass spectrometry as a new analytical method to characterize the proteome of the apo B carrying particles. Individual peptide components and comparison of molar ratios may improve risk prediction. In subfractions of LDL particles, the oxidation of phospholipids could provide novel insights on residual risk, despite the strong emphasis of almost all lipid management

guidelines on LDL-c as the preferred predictor of ASCVD risk as well as treatment targets. Our current understanding and recent evidence favor apo B as a superior marker of risk and therapeutic target.

Behbodikhah J, Ahmed S, Elyasi A *et al.* Apolipoprotein B and Cardiovascular Disease: Biomarker and Potential Therapeutic Target. Metabolites 2021; 11.

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