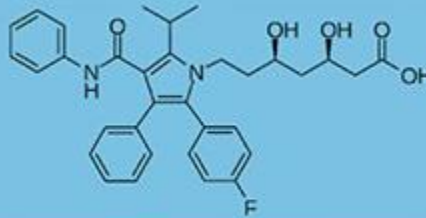


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IAS STATIN
NEWSLETTER



A CURATED WEEKLY UPDATE OF ALL STATIN PUBLICATIONS

Update - Week 05, 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

Fact or fiction? Statins pleiotropic properties

Retrospective analysis of the major statin outcome trials suggested benefits beyond their potent LDL-c lowering properties. These "pleiotropic" effects have attracted intense interest and discussions since statins were introduced over 30 years ago. Notably, the quicker and more significant cardiovascular benefit, beyond what was expected of the LDL-c lowering effect combined with an unexpected reduction of ischemic strokes in the SPARCL study, provided indications that statins were able to do more. Suggested potential mechanisms included plaque stabilization, mitigating inflammation, and vascular reactivity. There is a substantial body of evidence to support the pleiotropic effects, and an equally expanding body of clinical data pointed to a more nuanced interpretation of the statin pleiotropy. This review provides an unbiased update on the current understanding of statin's pleiotropic effects, including available clinical evidence and recommendations for future research to address statin pleiotropy questions.

Yu D, Liao JK. **Emerging views of statin pleiotropy and cholesterol lowering.** Cardiovascular research 2021. <http://www.ncbi.nlm.nih.gov/pubmed/?term=33533892>

The role of statins after Intracerebral haemorrhages (ICH)

The European Stroke organization prioritized research on the role of statins post-ICH. In this German ICH registry, a retrospective observational analysis was conducted to evaluate the benefits or harms when patients that suffered an acute ICH (re)started statins. In total 1275 ICH patients had data on statin use. At admission, 21.7% were using statins and were observed to have an increased risk for lobar vs. non-lobar ICH; OR 1.56 (1.03-2.40; P=0.038). Patients that started statin while admitted for the acute event had an increased peak peri hemorrhagic edema (PHE); Beta=0.12, SE=0.06, P=0.008). Post-stroke seizures were not significantly different between the two groups. Statin users: 11.5% versus no statins: 7.8%, sub-distribution HR: 1.15 (0.80–1.66; P=0.512). Statin use was associated with a non-significant trend for less CVD complications; HR: 0.60 (0.36-1.02, P=0.058) Functional recovery (after 12 months) was superior in statin users as well, 55.7% vs. 45.0%; OR:1.67 (1.09-2.56; P= 0.019). The Authors suggest not start statins during the first days of admission to avoid an increase in edema; however, those that used statins prior to hospital admission could safely continue taking them. Starting statins at discharge could reduce CVD events and improve functional discovery.

Sprügel MI, Kuramatsu JB, Volbers B *et al.* **Impact of Statins on Hematoma, Edema, Seizures, Vascular Events, and Functional Recovery After Intracerebral Hemorrhage.** Stroke 2021:Strokeaha120029345. <http://www.ncbi.nlm.nih.gov/pubmed/?term=33517701>

Comparing outcomes in MINOCA patients with and without AMI

Patients with non-obstructive coronary artery disease (MINOCA) diagnosed with AMI, based on coronary angiography and elevated plasma troponin were compared with MINOCA patients without AMI. Data collected in The Veterans Affairs (VA) Clinical Assessment, Reporting and Tracking (CART) program were used to in patients that had coronary angiography (CAG) between 2008 – 2017. Propensity matched patients were compared for MACE (MACE: mortality, myocardial infarction, and revascularization) within one year. Troponin assessment, before CAG, was available for 2 924 patients; 1 986 patients had elevated troponin of those 1908 were analyzed after propensity score matching. MACE risk was significantly increased in troponin-positive patients, HR= 2.37 (1.67-3.34). This risk was significantly less when patient used statins or ACEi, HR= 0.32 (0.22-0.49) and HR= 0.49 (0.32-0.75) respectively. The use of P2Y12 inhibitor, calcium-channel, and beta-blocker therapy was not associated with outcomes. MINOCA should be considered a significant risk factor

for mortality and morbidity; the observed 12-month mortality rate was 6%. The authors suggested that the discrepancy in MACE outcomes between statins and ACEi vs. calcium blockers and Beta-blocker could result from pleiotropic, anti-inflammatory properties of ACEi statins.

Kovach CP, Hebbe A, O'Donnell CI *et al.* Comparison of Patients With Nonobstructive Coronary Artery Disease With Versus Without Myocardial Infarction (From the VA Clinical Assessment Reporting and Tracking [CART] Program). *Am J Cardiol* 2021.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=33539858>

Comparing atorvastatin (40-80 mg) and rosuvastatin 20 mg in Korean post AMI patients

The Korea Acute Myocardial Infarction (KAMIR) Registry is a valuable source of information on Asian – Korean AMI patients. This study evaluated differences in the effect of high-intensity atorvastatin or rosuvastatin use on new-onset diabetes mellitus (NODM) and MACE (death, myocardial infarction, and revascularizations). Data for the KAMIR registry were collected between November 2011 and October 2015. For this analysis, 13, 104 AMI patients who used atorvastatin (40-80 mg) or rosuvastatin (20 mg) were included. Patients were comparable at baseline; event-free (NODM) survival, three years after AMI, were comparable between atorvastatin and rosuvastatin users, 92,5% vs. 90% respectively (P=0.555). this was similar for AMCE free survival, 89.0% vs. 89.6% (P=0.662). Based on a multivariate Cox, both rosuvastatin (20mg) and atorvastatin (40-80 mg) showed similar outcomes for AMCE free survival and NODM development and suggested clinical equivalence in secondary prevention.

Choi JY, Choi CU, Choi BG *et al.* New onset diabetes mellitus and cardiovascular events in Korean patients with acute myocardial infarction receiving high-intensity statins. *BMC pharmacology & toxicology* 2021; 22:11. <http://www.ncbi.nlm.nih.gov/pubmed/?term=33541430>

Pravastatin in pre-eclampsia prevention - The INOVASA study

The Indonesian INOVASIA study is an ongoing multicentre randomized, open controlled trial of pravastatin to prevent preeclampsia. This report evaluated the effects of pravastatin on VEGF, IL-6, ET-1, and NO, markers of inflammation and endothelial function. Included were 74 patients at high risk for developing preeclampsia. Pravastatin (2 x 20 mg /day) was used by 38 women and compared with 38 control patients. The medication was started week 14-20 and continued until delivery. Blood samples were drawn prior to starting the medication and just before delivery. All studied biomarkers improved in the patients that used pravastatin but remained stable or detoured in the control patients. Comparing pravastatin

use with no use was associated with the following changes. IL6: 191.87 ± 82.99 vs. 151.85 ± 48.46 , ($p=0.013$) no significant changes in control group. ET1 3.64 ± 0.85 vs. 3.01 ± 0.74 , ($p=0.006$) no significant changes in control group. NO increased in patients using pravastatin 11.30 (17.43) vs. 41.90 (53.18), $p=0.044$). Patients in the control group showed significant reductions in NO 38.70 (34.80) vs. 10.03 (26.96), $p=0.002$. VEGF a non-significant increasing trend in the pravastatin users 3.22 (0.62) vs. 3.28 (0.75), $p=0.402$, while an decreasing trend was noted in the control group 3.38 (0.83) vs. 3.06 (0.74), $p=0.287$. The preliminary findings in this small, randomized trial support the use of pravastatin 40 mg in women at risk for preeclampsia. The changes observed in inflammation and endothelial cell showed significant improvements vs. no change or even worsening of these markers was observed in women allocated to placebo. Outcome data successful pregnancies and mortality + morbidity of mother and child will provide clinical evidence on the impact of pravastatin on the prevention of preeclampsia.

Akbar MIA, Yosediputra A, Pratama RE *et al.* Pravastatin suppresses inflammatory cytokines and endothelial activation in patients at risk of developing preeclampsia: INOVASIA study. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet 2021:1-8.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=33522342>

Relevant publications

1. Akbar MIA, Yosediputra A, Pratama RE *et al.* Pravastatin suppresses inflammatory cytokines and endothelial activation in patients at risk of developing preeclampsia: INOVASIA study. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet 2021:1-8. <http://www.ncbi.nlm.nih.gov/pubmed/?term=33522342>
2. Jia Y, Wen J, Qureshi R *et al.* Effect of redundant clinical trials from mainland China evaluating statins in patients with coronary artery disease: cross sectional study. Bmj 2021; 372:n48. <http://www.ncbi.nlm.nih.gov/pubmed/?term=33531350>
3. Zeller M, Lambert G, Farnier M *et al.* PCSK9 levels do not predict severity and recurrence of cardiovascular events in patients with acute myocardial infarction. Nutrition, metabolism, and cardiovascular diseases : NMCD 2020. <http://www.ncbi.nlm.nih.gov/pubmed/?term=33546945>

4. Tejera E, Pérez-Castillo Y, Chamorro A *et al.* A Multi-Objective Approach for Drug Repurposing in Preeclampsia. Molecules (Basel, Switzerland) 2021; 26. <http://www.ncbi.nlm.nih.gov/pubmed/?term=33546161>
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13. Farnier M, Zeller M, Masson D, Cottin Y. Triglycerides and risk of atherosclerotic cardiovascular disease: An update. Arch Cardiovasc Dis 2021. <http://www.ncbi.nlm.nih.gov/pubmed/?term=33546998>
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Basic Science publications

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2. Koç O, Tüz HH, Ocak M *et al.* Can Combination of Simvastatin and Melatonin Create a Synergistic Effect on Bone Regeneration? Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons 2021. <http://www.ncbi.nlm.nih.gov/pubmed/?term=33524327>
3. Jafari M, Hojati V, Khaksari M, Vaezi G. Simvastatin attenuates spatial memory impairment via inhibiting microgliosis and apoptotic cell death against ethanol induced neurotoxicity in the developing rat hippocampus. Brain Res 2021:147341. <http://www.ncbi.nlm.nih.gov/pubmed/?term=33548270>
4. Ghanem HA, Nasr AM, Hassan TH *et al.* Comprehensive Study of Atorvastatin Nanostructured Lipid Carriers through Multivariate Conceptualization and Optimization. Pharmaceutics 2021; 13. <http://www.ncbi.nlm.nih.gov/pubmed/?term=33525642>
5. Baganha F, de Jong RCM, Peters EA *et al.* Atorvastatin pleiotropically decreases intraplaque angiogenesis and intraplaque haemorrhage by inhibiting ANGPT2 release and VE-Cadherin internalization. Angiogenesis 2021. <http://www.ncbi.nlm.nih.gov/pubmed/?term=33550461>
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