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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

Predictors of atorvastatin benefits to manage chronic subdural hematoma

Chronic subdural hematoma (CSDH) is not an uncommon type of intracranial hemorrhage in elderly patients. Surgical intervention is the standard therapeutic approach, but due to post-surgical complications and a high recurrence rate (up to 25%), non-invasive strategies have been evaluated. Atorvastatin use has been associated with improved outcomes and reduced recurrences in several studies. In this retrospective, observational analysis predictive factors for atorvastatin benefits were queried. A total of 89 moderate CSDH patients from multiple neurological surgery centers were included. Over a follow-up period of 24 weeks, 11 patients were surgically treated due to worsening of their neurological condition; this occurred after a median follow-up period of 12 days (2-27 days). Predictors of beneficial outcomes with atorvastatin, based on univariate and multivariate analyses, and confirmed by ROC curves, were high-density hematoma, basal cistern compression, and hematoma volume. Zhang X, Wang D, Tian Y *et al.* Risk Factors for Atorvastatin as a Monotherapy for Chronic Subdural Hematoma: A Retrospective Multifactor Analysis. [Frontiers in aging](#)

neuroscience 2021; 13:726592. <http://www.ncbi.nlm.nih.gov/pubmed/?term=34539386>

Benchmarking 5 major guidelines for statin recommendations

Using data collected in a large prospective population study, the Rotterdam study, 5 different international guidelines for lipid management were benchmarked. Levels of evidence (LOE) and classes of recommendation for primary prevention of ASCVD using statins. The following 5 guidelines were included: the American Heart Association/American College of Cardiology/Multisociety, US Preventive Services Task Force, Department of Veterans Affairs/Department of Defense, Canadian Cardiovascular Society, and European Society of Cardiology/European Atherosclerosis Society Clinical Practice Guidelines. Although these recommendations in these guidelines were based on the same evidence, the outcomes per guideline: proportions of the population recommended statin therapy by LOE/class, sensitivity and specificity for CVD events, and numbers needed to treat at ten years varied greatly. statin initiation was recommended in 59.4%, 40.2%, 45.2%, 73.7%, and 42.1%, respectively. Sensitivity for CVD events for treatment recommendations supported with strong LOE/class in 86.3%, 69.4%, 74.5%, 93.3% and 66.6% for the 5 guidelines respectively. The highest specificity was observed for the USPSTF recommendations, 45.3%, and the ESC/EAS had the lowest score, 10%. The estimated numbers NNT for those with the strongest LOE/class ranged from 20 to 26 for moderate-intensity and 12 to 16 for high-intensity statins. The authors note that the different recommendations for eligibility and the use of high- or intermediate-dose statins varied significantly; these differences could contribute to the ambiguity of optimally treating primary prevention patients with statins. Harmonizing grading LOE and grading systems could re-enforce updated evidence-based recommendations. Pavlović J, Greenland P, Franco OH *et al.* Recommendations and Associated Levels of Evidence for Statin Use in Primary Prevention of Cardiovascular Disease: A Comparison at Population Level of the American Heart Association/American College of Cardiology/Multisociety, US Preventive Services Task Force, Department of Veterans Affairs/Department of Defense, Canadian Cardiovascular Society, and European Society of Cardiology/European Atherosclerosis Society Clinical Practice Guidelines. Circ Cardiovasc Qual Outcomes 2021;

14:e007183. <http://www.ncbi.nlm.nih.gov/pubmed/?term=34546786>

Comparing effects of different statin regimens on 5-year MACCE risk post-CABG

To determine the efficacy of different statin dosages in patients that had a CABG procedure. Data of patients were collected from the Samsung Medical Center institutional registry in Korea. In total 6 531 patients were stratified into four groups: 1. No or low-intensity statin (atorvastatin <10 mg; N=731). 2. Low to moderate-intensity statin (atorvastatin 10 mg;

N=2310). 3. High moderate-intensity statin (atorvastatin 10-20 mg; N=2404) and 4. High intensity statin (atorvastatin 40 mg; n=1086). The primary endpoint was a combined endpoint of MACCE after 5-years. No significant differences were observed between patients that used no or low-intensity statin and low to moderate-intensity statin. Patients on high-moderate intensity statins had a significantly lower risk compared to group 1 or 2. HR: 0.622 (0.479–0.807; p<0.001) this was comparable with the reduced risk observed in patients that used (the equivalent) of 40 mg atorvastatin, HR: 0.613 (0.421–0.894; p=0.011). No significant risk reduction was noted when group 4 was compared to group 3; HR: 0.987 (0.661–1.475; p=0.950). Using multivariable-cox and inverse probability weighing analyses showed similar results. The observed reduced risk for MACCE was not observed in patients that underwent CABG procedure for stable ASCVD.

Jang YH, Choi KH, Song YB *et al.* Effects of Statin Intensity on Long-Term Outcomes after Coronary Artery Bypass Grafting. The Annals of thoracic surgery 2021. <http://www.ncbi.nlm.nih.gov/pubmed/?term=34555373>

A pilot study to evaluate the use of rosuvastatin for VTE prophylaxis

This pilot study evaluated the potential anti-thrombotic effects of rosuvastatin in patients diagnosed with a newly diagnosed symptomatic proximal deep vein thrombosis (DVT) and/or pulmonary embolism (PE). All patients were treated with standard anticoagulation. Patients were randomized to rosuvastatin 20 mg/day or placebo for six months. Patients were recruited from six centers, and of the 1347 VTE patients were found eligible for this study, and 312 patients were randomized. During the 6-month follow-up, five recurrent VTE's were Registered. Three in the rosuvastatin-treated patients (two pulmonary embolisms and one DVT. In the control group, two patients developed recurrent thrombotic events (two pulmonary embolisms; p=0.68). One patient taking rosuvastatin experienced a major arterial event, vs. none in the control group. These outcomes support setting up a larger randomized controlled trial to explore the potential use of rosuvastatin for VTE prophylaxis.

Delluc A, Ghanima W, Kovacs MJ *et al.* Statins for venous event reduction in patients with venous thromboembolism: A multicenter randomized controlled pilot trial assessing feasibility. Journal of thrombosis and haemostasis : JTH 2021. <http://www.ncbi.nlm.nih.gov/pubmed/?term=34564938>

A randomized trial shows that atorvastatin can improve outcomes of hospitalized COVID-19 patients.

Most published data on potential benefits of statins for COVID-19 hospital admitted patients were observational studies. In this small randomized controlled trial, 40 adults hospitalized COVID-19 patients were allocated to atorvastatin + lopinavir/ritonavir or only lopinavir/ritonavir. The primary endpoint, length of hospital stay, was 9.75 days in the

control group and 7.95 days in patients on atorvastatin ($p=0.012$). The secondary outcomes (at day six of hospitalization) showed mixed results with a trend towards better outcomes for patients using atorvastatin. There are no significant differences between the two treatment arms for Interferon/immunoglobulin requirement (4 patients in the control group and three patients in the atorvastatin group, NS). Mechanical ventilation (one patient in the control group and none in the atorvastatin group, NS). Oxygen saturation (91.5% in the control group and 93.4% in the statin-treated patients, NS). The CRP plasma concentrations were significantly lower in the patients who were allocated atorvastatin (44.45 mg/dL in the control group and 22.9 mg/dL in the atorvastatin-treated patients, $p=0.01$). In this small, randomized study, the findings of several large observational studies that statin use was associated with improved outcomes, are not refuted. The small size and short duration warrant larger properly designed randomized placebo-controlled trials to confirm these promising findings.

Davoodi L, Jafarpour H, Oladi Z *et al.* Atorvastatin therapy in COVID-19 adult inpatients: A double-blind, randomized controlled trial. International journal of cardiology. Heart & vasculature 2021; 36:100875. <http://www.ncbi.nlm.nih.gov/pubmed/?term=34541293>

Relevant publications

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2. Sonaglioni A, Cara MD, Nicolosi GL *et al.* Rapid Risk Stratification of Acute Ischemic Stroke Patients in the Emergency Department: The Incremental Prognostic Role of Left Atrial Reservoir Strain. Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association 2021; 30:106100. <http://www.ncbi.nlm.nih.gov/pubmed/?term=34525440>
3. Shinohara K, Ikeda S, Enzan N *et al.* Efficacy of intensive lipid-lowering therapy with statins stratified by blood pressure levels in patients with type 2 diabetes mellitus and retinopathy: Insight from the EMPATHY study. Hypertension research : official journal of the Japanese Society of Hypertension 2021. <http://www.ncbi.nlm.nih.gov/pubmed/?term=34526672>
4. Santoleri F, Romagnoli A, Costantini A. Adherence and persistence in the use of statins and ezetimibe over 8 years in a real-life study. Current medical research and opinion 2021:1-6. <http://www.ncbi.nlm.nih.gov/pubmed/?term=34515600>

5. Rey JR, Merino Llorens JL, Iniesta Manjavacas Á M *et al.* Influence of statin treatment in a cohort of patients admitted for COVID-19. Med Clin (Barc) 2021. <http://www.ncbi.nlm.nih.gov/pubmed/?term=34511251>
6. Oyama K, Giugliano RP, Tang M *et al.* Effect of evolocumab on acute arterial events across all vascular territories : results from the FOURIER trial. Eur Heart J 2021. <http://www.ncbi.nlm.nih.gov/pubmed/?term=34537830>
7. Moon IT, Kang SH, Lee W *et al.* Impact of statin intensity on adverse cardiac and cerebrovascular events in older adult patients with myocardial infarction. Journal of geriatric cardiology : JGC 2021; 18:609-622. <http://www.ncbi.nlm.nih.gov/pubmed/?term=34527027>
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9. Jamialahmadi T, Baratzadeh F, Reiner Ž *et al.* The Effects of Statin Dose, Lipophilicity, and Combination of Statins plus Ezetimibe on Circulating Oxidized Low-Density Lipoprotein Levels: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Mediators Inflamm 2021; 2021:9661752. <http://www.ncbi.nlm.nih.gov/pubmed/?term=34526854>
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11. Handhe A, Viljoen A, Wierzbicki AS. Elevated Lipoprotein(a): Background, Current Insights and Future Potential Therapies. Vasc Health Risk Manag 2021; 17:527-542. <http://www.ncbi.nlm.nih.gov/pubmed/?term=34526771>
12. Gong Z, Zhan D, Nie M *et al.* Dexamethasone enhances the efficacy of atorvastatin in inhibiting excessively inflammation-induced abnormal angiogenesis by regulating macrophages. Journal of neuroinflammation 2021; 18:203. <http://www.ncbi.nlm.nih.gov/pubmed/?term=34526068>
13. Gao F, Wang ZJ, Ma XT *et al.* Effect of alirocumab on coronary plaque in patients with coronary artery disease assessed by optical coherence tomography. Lipids Health Dis 2021; 20:106. <http://www.ncbi.nlm.nih.gov/pubmed/?term=34511134>
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