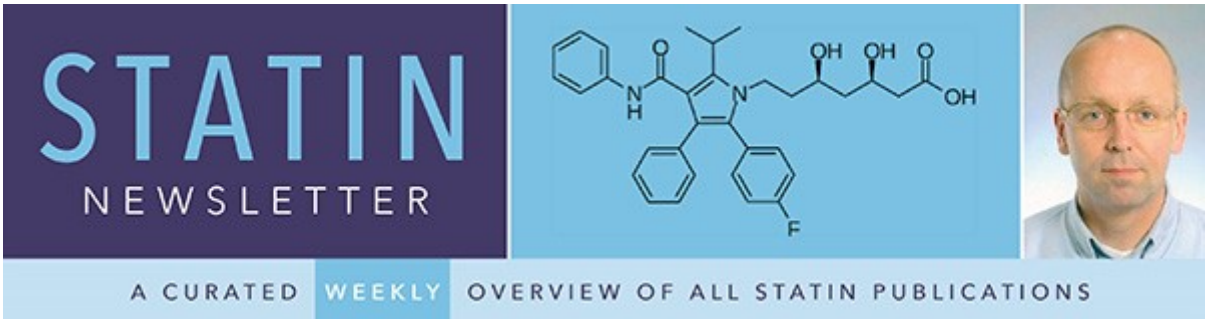

Update week 19 & 20 - 2022

Dr. Peter Lansberg is a Dutch lipidologist, educator and innovator. He has been instrumental in setting up The Dutch National Lipid Clinic Network, the Dutch Lipid Clinic Criteria for Familial Hypercholesterolemia (FH), and the Dutch National FH screening program

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The Statin Newsletter will keep you up-to-date with all recent statin publications. Based on a curated approach to select relevant articles.

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Key Publications

1. **Apo B a better marker!**
2. **Reduced HF complications when statins are started in a primary prevention setting**
3. **Dose of atorvastatin relevant when aiming to reduce CI-AKI**
4. **Statins do prevent ICH risk when started early**
5. **Glaucoma no affected by statin use**

Apo B superior to LDL-c for ASCVD and residual risk assessment

Should we shift from LDL-C to apo B for thresholds and targets? The findings of this small study confirm the superiority of the latter over the first. Patients treated with statins (N=131) and information on the extent of coronary atherosclerosis (AS) were used to determine which of the two biomarkers provided the most robust association. The severity of AS was significantly associated with higher plasma concentrations of Apo B (Ptrend=0.012). No significant association was observed for LDL-c (Ptrend =0.585). Using a multivariate statistical analysis, the residual risk for coronary AS showed a significant association with apo B (Ptrend =0.011). This resulted in a 45% increased residual risk of CAD per unit increment in natural log-transformed apo B (Ptrend <0.05). No significant association was observed for LDL-c (Ptrend =0.437). Similar outcomes were observed after stratified and sensitivity analyses. These findings support earlier recommendations to use apo B instead of LDL-c as a superior marker for residual risk and ASCVD.

Yao T, Lu W, Ke J *et al.* Residual Risk of Coronary Atherosclerotic Heart Disease and Severity of Coronary Atherosclerosis Assessed by ApoB and LDL-C in Participants With Statin Treatment: A Retrospective Cohort Study. Frontiers in endocrinology 2022; 13:865863. http://www.ncbi.nlm.nih.gov/pubmed/?term=35573992

Statins started in primary prevention reduce HF related outcomes

The role of statin in patients with advanced heart failure (HF) is doubtful after the randomized controlled outcome trials (CORONA and GISI-HF) were unable to show benefits in patients using rosuvastatin compared to placebo. Statins seem to provide benefits in the early stages of HF or prevent HF-related complications. Data collected in the International Survey of Acute Coronary Syndromes Archives showed that patients who presented with ACS as a first ASCVD event (N=15 542) were using statins before their hospital admission did better compared to patients who were not using statins when evaluated for HF-related complications. Admissions for acute HF were reduced in the statin users, RR 0.72 (0.62-0.83) and a 4.3% absolute risk reduction. This was independent of age and sex. Lower 30-day mortality in patients that presented with acute HF was noted as well. A RR of 0.71 (0.50-0.99) and an absolute risk reduction of 5.2%. Despite the limitations of this study, highlighted in the accompanying editorial, the findings of this registry show that patients who started statin as a primary prevention strategy ended up with significantly reduced risk for both atherogenesis and its consequences, regardless of their age.

Bugiardini R, Yoon J, Mendieta G *et al.* Reduced Heart Failure and Mortality in Patients Receiving Statin Therapy Before Initial Acute Coronary Syndrome. J Am Coll Cardiol **2022; 79:2021-2033. http://www.ncbi.nlm.nih.gov/pubmed/?term=35589164**

Schocken DD. Registry Evidence for Modulation of the Acute Ischemic Heart Disease Pathway: Statins Prevent Heart Failure? J Am Coll Cardiol **2022; 79:2034-2036. http://www.ncbi.nlm.nih.gov/pubmed/?term=35589165**

To prevent CI-AKI a high dose of atorvastatin is superior to a lower dose

Contrast imaging provides valuable insights into the underlying vascular pathology and is indispensable to determining if invasive interventions are necessary. Contrast-induced acute kidney injury (CI-AKI) is a serious complication not infrequently observed in older patients or those with impaired renal function. Atorvastatin, a lipophilic statin, seems to protect from contrast-induced renal toxicity. In this study, the dose-dependent effect of atorvastatin was evaluated. In this small Chinese study, 300 patients scheduled for coronary CT imaging were randomized to 40 mg or 20 mg of atorvastatin. Patients were given the statin one day before the scheduled procedure and for an additional four consecutive days after. Renal injury was significantly reduced in patients that received 40 mg (2%) compared to those that used 20 mg of atorvastatin (8%) (X2 = 6.62, P= 0.010). At baseline, no differences were observed in the plasma concentrations of Scr, BUN, CysC, hs-CRP, and IL-6. After the CT evaluation (72hrs), Scr, BUN, CysC, hs-CRP, and IL-6 increased, and eGFR decreased in the control group (atorvastatin 20 mg). In contrast with the patients that used atorvastatin 40 mg in whom all related renal biomarkers remained stable and significantly better compared to the control group. This study shows the importance of not only using atorvastatin to prevent CI-AKI but that using a high dose of atorvastatin seems superior. The short duration of the intervention supports the role of pleiotropic effects of statins for the prevention of CI-AKI, which is most likely related to anti-inflammatory benefits.

Yan SX, Gao M, Yang TH *et al.* The preventive effects of different doses of atorvastatin on contrast-induced acute kidney injury after CT perfusion. Journal of clinical laboratory analysis **2022:e24386. http://www.ncbi.nlm.nih.gov/pubmed/?term=35582743**

Can statins prevent intracerebral hemorrhage risk?

The Danish stroke registry is one of the largest national registries, collecting hospital admission data and long-term follow-up information of Danish patients that suffered a cerebral stroke. Data from this registry was combined with a medication registry containing all dispensed prescriptions from community pharmacies since 1995. The 16 235 patients in this registry suffered an intracerebral hemorrhage (ICH), compared to 640 943 controls from the general population. The primary aim of this analysis was to determine the risk of intracerebral hemorrhage (ICH) in patients using statins. Statins were used by 25.9% of the ICH patients and 24.5% of the controls. Overall the relative risk of ICH was reduced by 26% in the statins users; aOR: 0.74 (0.71-0.78). The duration of statin use determined ICH risk as well. Patients using statins < 1year had and aOR of 0.86) (0.81-0.92) 0.92; ≥1 to <5 years:

aOR: 0.72 (0.68-0.76; ≥5 to <10 years; aOR: 0.65; (0.60-0.71), and ≥10 years of use, aOR: 0.53 (0.45-0.62; P for trend <0.001). statin intensity showed similar trends; high intensity therapy: <1 year of use, aOR: 0.78 (0.66-0.93); ≥10 years of use aOR: 0.46 (0.33-0.65; P for trend 0.001). The authors concluded that the results of their analysis supported the use of statins to reduce the risk of ICH (Class II evidence). Duration of statin use was correlated with a reduced ICH risk as well.

Rudolph DA, Hald SM, García Rodríguez LA *et al.* **Association of Long-term Statin Use With the Risk of Intracerebral Hemorrhage: A Danish Nationwide Case-Control Study.** Neurology 2022. http://www.ncbi.nlm.nih.gov/pubmed/?term=35577575

Can statins improve or worsen glaucoma?

Statins could protect or worsen glaucoma in patients diagnosed or at risk of this common age-related disorder. The rates of structural and functional loss in patients with glaucoma were evaluated in the Duke Glaucoma registry. In this retrospective cohort study, patients with, or suspected of, open-angle glaucoma were entered into the registry. Clinically relevant ocular parameters associated with glaucoma were measured. For this analysis, patients were divided into statin users and those that did not take statins. The duration of statin use was recorded as well. In total, 1978 patients were followed for an average time of 4.7±2.0 years. Statins were used by 775 subjects (1179 eyes). No differences in the rates of glaucoma-related changes were seen between the statin users versus the control group. Compared were the mean deviation (MD), −0.07±0.16 dB/year vs −0.07±0.15 dB/year (p=0.873) respectively and retinal nerve fiber layer thickness: −0.70±0.60 µm/year vs −0.70±0.61 µm/year (p=0.923), respectively. Based on the findings of this registry, no signal that indicated either a decrease or increase in glaucoma-related signs were observed.

Kang JM, Jammal AA, Medeiros FA. **Association between statin use and rates of structural and functional loss in glaucoma.** Br J Ophthalmol 2022. http://www.ncbi.nlm.nih.gov/pubmed/?term=35537803

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Basic Science

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