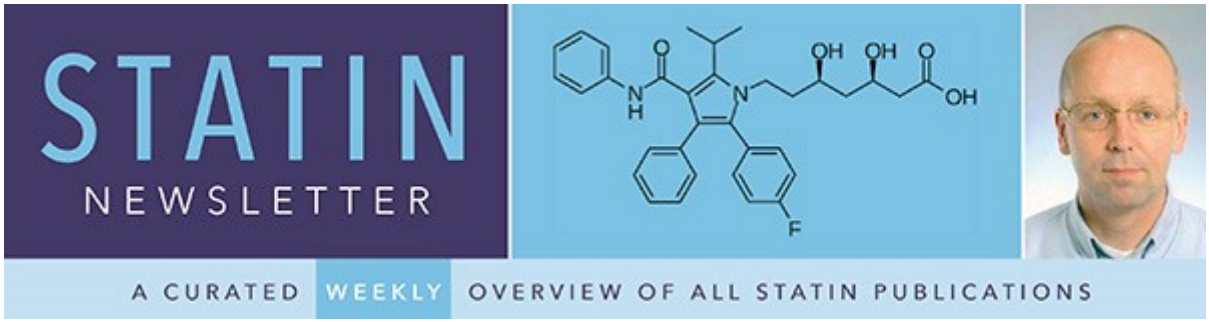

Update week 35 & 36 - 2022

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. **Review preserving venous graft patency**
2. **Statins for NAFLD patients?**
3. **Are guideline LDL-c targets right?**
4. **Ator vs Rosu in primary PCI**
5. **Dialysis patients and statins**

Persevering saphenous vein graft patency

This review explores current optimal strategies to prevent saphenous vein graft failure. The three distinct pathophysiological processes related to graft occlusion are acute thrombosis, intimal hyperplasia, and accelerated atherosclerosis. Local inflammation and prothrombotic cascades are crucial components to trigger graft failure. A better understanding of these processes resulted in preserved graft patency. Aspirin and long-term statin use have resulted in significant improvement in improved saphenous graft survival.

Guida GA, Angelini GD. Pathophysiology and Mechanisms of Saphenous Vein Graft Failure. Brazilian journal of cardiovascular surgery 2022; 37:32-37. http://www.ncbi.nlm.nih.gov/pubmed/?term=36053999

Meta-analysis of statins in NAFLD

In patients with liver disease, statin use was contra-indicated, and statins were stopped when transaminases increased to >3 times the upper limit of normal; this systematic review and meta-analysis evaluates the benefits of statins in patients with NAFLD and NASH. Both biochemical and histological characteristics are evaluated. Included in this analysis were 13 studies, 4 randomized clinical trials, and 9 observational studies. NAFLD was diagnosed by imaging or liver biopsies. Significant improvements in lipids, transaminases, and hepatic steatosis were observed in all studies. Hepatic steatosis grade improved by a standard

mean difference (SMD) of -1.73 (2.1-1.35; $p < 0.00001$; I^2=98%). In statin users, the NAFLD score also got better; SMD -1.09 (-1.39-0.79; $p < 0.00001$; I^2=93%). These findings confirm earlier meta-analyses and reviews are indicating that statins reduce transaminases and improve liver histology in NAFLD. Patients with NAFLD are at increased risk for ASCVD; using statins would not only improve NAFLD and reduce CVD risk.
Boutari C, Pappas PD, Anastasilakis D, Mantzoros CS. **Statins' efficacy in non-alcoholic fatty liver disease: A systematic review and meta-analysis**. Clinical nutrition (Edinburgh, Scotland) 2022; 41:2195-2206. http://www.ncbi.nlm.nih.gov/pubmed/?term=36081293

Reformulating LDL-c targets based on current trial evidence

An alternative approach to determine LDL-c treatment threshold is presented in this review using a simple mathematical formula, the efficacy of different therapeutic interventions as well as lipid targets (LDL-c, Non-HDL, and Apo B). The current primary prevention LDL-c target of 100 mg/dL (2.6 mmol/L) is suggested to be ineffective and lacking credibility. The best overall target of 70 mg/dL (1.8 mmol/L) or an LDL-c reduction of at least 50%. Non-HDL-C is a less precise and efficacious therapeutic target as well. In very high-risk patients, aiming for an LDL-c target of 55 mg/dL (1.4 mmol/L) result in only a small improvement. This could be an essential alternative target for patients with high case fatality risk. Apo lipoprotein B is a superior target compared to LDL-c; it is more homogenous and can be accurately measured in hypertriglyceridemia patients.
Durrington PN, Bashir B, Soran H. **What should be the goal of cholesterol-lowering treatment? A quantitative evaluation dispelling guideline myths.** Curr Opin Lipidol 2022; 33:219-226. http://www.ncbi.nlm.nih.gov/pubmed/?term=36082945

Comparing single tablet of atorvastatin vs rosuvastatin for primary PCI

Similar to the ARMYDA-Recapture trial, patients admitted with an acute STEMI and scheduled for a primary PCI are randomly assigned to a single tablet of atorvastatin 80 mg (N=33), 40 mg of Rosuvastatin (N=33) or the control group (N=33) in the ER. The endpoints, post-interventional thrombolysis in myocardial infarction (TIMI) flow grade, and corrected TIMI frame count (CTFC) were recorded, and ST-segment resolution was measured. A final TIMI flow grade 3 was achieved in 32 (97.0%) patients in the rosuvastatin group and 28 (84.8%) patients in the atorvastatin group compared with only 25 (75.8%) patients in the control group ($p = 0.014$). Peak CK-MB in the rosuvastatin group (263.2 [207.2–315.6]) and the atorvastatin group (208 [151.0–314.1]) was lower compared to that in the control group (398.4 [303.9–459.3]); $p < 0.001$. Conclusions: A single dose of 80 mg of atorvastatin prior to primary PCI in STEMI patients showed better improvement in microvascular myocardial perfusion compared to 40 mg of rosuvastatin.
Adel EM, Elberry AA, Abdel Aziz A *et al.* **Comparison of the Treatment Efficacy of Rosuvastatin versus Atorvastatin Loading Prior to Percutaneous Coronary Intervention in ST-Segment Elevation Myocardial Infarction.** Journal of clinical medicine 2022; 11. http://www.ncbi.nlm.nih.gov/pubmed/?term=36079090

Dialysis patients with concomitant PAD benefit from statins

In the 4D and AURORA studies, statin use in patients with renal failure failed to show benefits. In this retrospective study cohort using data from the Taiwan National Health Insurance Research Database, Chinese renal failure patients with concomitant peripheral artery disease (PAD) were analyzed. A total of 20 731 hemodialysis patients diagnosed with PAD and dyslipidemia were identified between January 1, 2001and December 31, 2013. For the final analysis 10, 767 patients were included. Data were analyzed from June 8, 2021, to June 2, 2022. Primary outcomes were all-cause death, endovascular therapy (EVT), and amputation. Secondary endpoints included CV events (CV death, acute myocardial infarction, ischemic stroke, and hospitalization for heart failure), major adverse limb events (new-onset claudication, new-onset critical limb ischemia, EVT, and nontraumatic amputation), and all-cause readmission. Outcomes were examined at 1 year and 3 years of follow-up. Statin users and non-statin users were propensity score matched on a 1:1 ratio. A defined daily dose (DDD) approach was used to evaluate whether the association of statin

therapy with the risk of primary outcomes was dose-dependent. The incidence and risk of CV and all-cause death were significantly lower in the statin group vs. the non-statin group at 3 years of follow-up (CV death: 611 patients [18.9%] vs. 685 patients [21.2%]; hazard ratio [HR], 0.86 [95%CI, 0.77-0.96];P = .008; all-cause death: 1078 patients [33.3%] vs. 1138 patients [35.2%]; HR, 0.92 [0.84-0.996]; P = .04). Statin use was also associated with a significantly lower incidence and risk of the composite adverse limb outcome of EVT and amputation at 3 years of follow-up (314 patients [9.7%] vs. 361 patients [11.2%]; HR, 0.85 [0.73-0.99]; P = .04). Results of subgroup analyses were consistent with those of the primary analysis across all subgroup variables. In the adjusted dose-response analysis, the risk reduction associated with statin use increased in a dose-dependent manner for both all-cause death (HR: 0.95 for DDD <0.50, 0.92 for DDD 0.50-0.99, 0.85 for DDD 1.00-1.49, and 0.79 for DDD 1.50; P = .002 for trend) and the composite outcome of EVT and amputation (sub distribution HR: 0.79 for DDD <0.50, 0.78 for DDD 0.50-0.99, 0.82 for DDD 1.00-1.49, and 0.58 for DDD 1.50; P = .002 for trend) compared with no statin therapy. These findings suggest that statin therapy may have protective CV and limb benefits for renal failure patients with concomitant PAD.

Lo HY, Lin YS, Lin DS *et al.* **Association of Statin Therapy With Major Adverse Cardiovascular and Limb Outcomes in Patients With End-stage Kidney Disease and Peripheral Artery Disease Receiving Maintenance Dialysis.** JAMA network open 2022; 5:e2229706. http://www.ncbi.nlm.nih.gov/pubmed/?term=36048442

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Basic Science

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