



Update week 31 & 32 - 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

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. **Should statins be started ASAP in ACS patients**
2. **Surprising effects of statins on sarcopenia in HF**
3. **Canadian guidelines on pediatric lipid management**
4. **Impact of high intensity statins on structural stress in plaque architecture**
5. **Drug interactions with Paxlovid and statins**

Increased survival benefit if statins are administered < 24 hrs. in ACS patients.

Should statins be started < 24hr after admission in patients with severe ACS (Killip class III/IV)? This Chinese national registry of ACS patients with advanced Killip class and early statin initiation were compared to patients with similar Killip class events, in whom statins were not prescribed <24hrs. In the registry, data of 104 516 ACS patients were re-evaluated. There were 12 149 Patients with Killip class III/IV, and 89% started statins early. Using a Multivariate-adjusted logistic regression model, patients with early statin use were compared to patients that started statins later. The study endpoints were: (i) in-hospital mortality and ischemic events; (ii) the dose effect of statins on mortality, and (iii) the interaction between LDL-C levels and statins on mortality. All outcomes showed the benefit of early statin initiation. Mortality OR 0.31 (0.25-0.39); Ischemic events OR: 0.50 (0.33-0.77). This was noted for in-hospital mortality in patients receiving low-moderate dosages as well as a short-term survival benefit. Intriguingly the short-term mortality benefit was independent of LDL-c, indicating that potential pleiotropic effects of statins contributed to the observed protective effects. In this study, early statin administration was associated with substantial benefit in ACS patients with impaired cardiac function Song X, Zhou X, Li Z *et al.* **Early Statin Therapy and In-Hospital Outcomes in Acute Coronary Syndrome Patients**

Presenting with Advanced Killip Class at Admission: Findings from the CCC-ACS Project.
Am J Cardiovasc Drugs 2022. <http://www.ncbi.nlm.nih.gov/pubmed/?term=35962306>

HF patients using statins less likely to develop sarcopenia

Increased survival benefit if statins are administered < 24 hrs. in ACS patients.

In heart failure (HF) patient's sarcopenia (muscle atrophy that occurs with aging and/or immobility) contributes significantly to impaired cardiac output and poor prognosis. Statin use is postulated as a potential risk factor for developing sarcopenia. In this cross-sectional study, 136 HF patients were recruited from an HF outpatient clinic of a Portuguese university hospital. A total of 25 (18.4%) individuals were categorized as sarcopenic, ranging from 12.2% in

Those < 65 years vs. 30.4% >65 years ($p = 0.009$). Men were less likely to be sarcopenic (3.3%) vs. 47.8% in women ($p < 0.001$). Severe sarcopenia accounted for 7.4% of the sample, and sarcopenic obesity was present in 5.1% of the participants. Age was positively associated with sarcopenia; for each year, a 9% increase in the likelihood of being sarcopenic was observed OR = 1.09 (1.01-1.17). Each 1 Kg.m⁻² BMI increase was associated with a 21% decrease in the likelihood of sarcopenia OR = 0.79 (0.65-0.96). Patients using five or more medicines had a markedly increased risk of developing sarcopenia, OR = 26.8 (2.01-359.26). Statins were inversely associated with sarcopenia OR = 0.03 (0.01-0.30). A possible suggestion for these surprising findings is that the pleiotropic effects of statins on endothelial function contributed to better neuromuscular fitness.

Valdivieso R, Sousa-Santos AR, Azevedo LF *et al.* **Statins are associated with reduced likelihood of sarcopenia in a sample of heart failure outpatients: a cross-sectional study.** BMC Cardiovasc Disord 2022; 22:356. <http://www.ncbi.nlm.nih.gov/pubmed/?term=35931947>

Canadian paediatric dyslipidemia guidelines – Update for clinical practice

Familial hypercholesterolemia (FH) and other high-risk primary and secondary pediatric lipid disorders are not uncommon. A timely detection/diagnosis, followed by treatment, could significantly impact atherosclerosis and ASCVD risk. Although lifestyle modifications with dietary changes remain the basis when managing pediatric dyslipidemia, medication can be prescribed depending on the severity and ASCVD risk. Well-established lipid-lowering drugs such as statins have been successfully tested in numerous clinical trials with undisputable significant improvement and minimal side effects or tolerability issues. Novel potent LDL-c lowering medications such as PCSK9ab are now in the process of being evaluated in pediatric trials, potentially supporting the use of these new and very effective LDL-c drugs in the near future. These could be of significant value in children with severe heterozygous or homozygous FH. The authors underline that the development of knowledge translation strategies is urgently needed to improve the screening and detection of lipid disorders in Canadian youth.

Khoury M, Bigras JL, Cummings EA *et al.* **The Detection, Evaluation, and Management of Dyslipidemia in Children and Adolescents: A Canadian Cardiovascular Society/Canadian Pediatric Cardiology Association Clinical Practice Update.** Can J Cardiol 2022; 38:1168-1179. <http://www.ncbi.nlm.nih.gov/pubmed/?term=35961755>

High intensity statin improves plaque architecture by reducing structural stress

Arguments for using high-intensity statins (HIS) are reflected in all lipid management guidelines, predominantly based on reducing ASCVD complications in those that use high-dose, high-intensity statins. The authors of this article share interesting data on the impact of HIS on plaque structural stress (PSS), a major cause of plaque rupture and subsequent ASCVD events. Changes in PSS, plaque size, and composition were obtained from 7348 baseline and follow-up virtual histology intravascular ultrasound images (IVUS) in patients that were treated with standard medical therapy ($n=18$); the control group and patients using HIS: Atorvastatin 80 mg ($N=20$) or rosuvastatin 40 mg ($N=22$). A significant difference was noted between HIS use and the control patients on PSS ($P<0.001$). PSS_{peak} increased significantly in the control lesions with plaque burden (PB) >60% ($p=0.04$); this was absent

in the patients using HIS. Changes in PSSpeak correlated poorly with changes in lumen and plaque area, plaque composition, or lipid-lowering. However, significant associations were noted with changes in lumen curvature, irregularity, and roughness ($P < 0.05$), all of which were reduced in HIS patients. In this observational study, HIS was associated with smoothing of plaques by reducing plaque/lumen roughness, irregularity, and curvature. This represents a novel mechanism whereby HIS may reduce PSS and may protect against plaque ruptures and MACE.

Gu SZ, Costopoulos C, Huang Y *et al.* High-intensity statin treatment is associated with reduced plaque structural stress and remodelling of artery geometry and plaque architecture. *Eur Heart J Open* 2021; 1:oeab039. <http://www.ncbi.nlm.nih.gov/pubmed/?term=35919883>

Paxlovid and statins – warning

COVID complications and ASCVd are closely interconnected. Patients at risk for CVD have a greater chance of hospital or ICU admission, and those infected with the SARS-CoV-2 virus are also at risk for cardiac complications. Currently, the use of Paxlovid is increasing based on the favorable outcomes in patients at risk for COVID complications. Both Paxlovid and statins are metabolized by Cytochrome P4507A (CYP 3A), which may result in significant drug interactions. Should statins be stopped when patients receive Paxlovid? The authors of this review would be more in favor of changing the statin type or dose reduction; a potential rebound effect of the cardiovascular system triggered by a sudden withdrawal of statins is thus avoided. Simvastatin and lovastatin should be substituted, e.g., pravastatin or Fluvastatin, while for patients using atorvastatin or rosuvastatin, a dose reduction is recommended. The treatment course of Paxlovid is 5-days; patients need to be instructed on potential signs or symptoms of harmful drug interactions and to contact their physician should they occur.

Vuorio A, Kovanen PT, Raal F. Cholesterol-lowering drugs for high-risk hypercholesterolemia patients with COVID-19 while on Paxlovid™ therapy. *Future Virol* 2022. <http://www.ncbi.nlm.nih.gov/pubmed/?term=35935448>

Relevant Publications

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Basic Science

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