



Update week 51 & 52 - 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. **European position paper on LDL-c lowering in post-ACS patients**
2. **Statins preventing hip fractures in diabetic patients**
3. **Update review on lipid management in children**
4. **Elevated ALT does not predict acute liver injury in statin users**
5. **Statin use in hemorrhagic stroke patients associated with reduced mortality**

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### Position paper LDL-c reduction post ACS

A position paper by representatives of the European Association of Preventive Cardiology and the European Society of Cardiology Working Group on Cardiovascular Pharmacotherapy recommends a 'strike early and strong' approach in patients after acute coronary syndrome (ACS). The authors use six lines of reasoning to support their recommendations. First, lower LDL-C is better. Second, getting the LDL-C to goals is critical. Third, recurrent ischaemic events occur early and before the time that step-wise increase of lipid-lowering therapies is achieved. Fourth, currently, patients are not discharged on optimal lipid-lowering therapy, and there is a lack of therapy changes on follow up when LDL-C goals are not achieved. Fifth, early and strong lipid-lowering therapy decreases plaque size. Sixth, this approach is likely to be safe. The authors recommend acute proprotein convertase subtilisin/kexin 9 (PCSK9) inhibitors as a novel strategy, especially in patients exhibiting high risk features such as multivessel coronary artery disease or polyvascular disease and patients with familial hypercholesterolemia. The authors state that all patients should be treated with a high intensity statin such as atorvastatin 80 mg. The authors also state that combination pills of high intensity statins and ezetimibe may improve adherence and LDL-C lowering. However, the position paper is not a guideline and has no levels of evidence or classes of recommendations. The authors

did not compare the speed of different LDL-C-lowering therapies and achievement of LDL-C goals and did not address cost effectiveness. A specialized secondary prevention clinic is recommended at 4–6 weeks to re-evaluate achieved LDL-C, treatment tolerability, and compliance. The authors did not give an LDL-C level at which de-escalation of triple therapy might occur. This position paper will be helpful for doctors and GPs looking after patients with ACS and also for patients. Krychtiuk KA, Ahrens I, Drexel H *et al.* **Acute LDL-C reduction post ACS: strike early and strike strong: from evidence to clinical practice. A clinical consensus statement of the Association for Acute CardioVascular Care (ACVC), in collaboration with the European Association of Preventive Cardiology (EAPC) and the European Society of Cardiology Working Group on Cardiovascular Pharmacotherapy.** *Eur Heart J Acute Cardiovasc Care* 2022; 11:939-949. <http://www.ncbi.nlm.nih.gov/pubmed/?term=36574353>

White HD. **Value of expert opinion in recommending early intensive lipid lowering in patients with ACS.** *Eur Heart J Acute Cardiovasc Care* 2022; 11:936-938. <http://www.ncbi.nlm.nih.gov/pubmed/?term=36574352>

### **Hip fracture risk reduced in diabetic patients using statins**

A study was conducted to investigate the association between statin use and hip fracture (HFX) risk among patients with type 2 diabetes mellitus (T2DM). The study was a retrospective Taiwan population-based propensity-matched cohort study using the Diabetes Mellitus Health Database from Taiwan National Health Insurance Research Database. After adjusting for multiple confounding factors, the results showed that statin use in T2DM patients was associated with a decreased risk of HFX with an adjusted hazard ratio of 0.69. A dose-response relationship was also identified, with the lowest risk of HFX among patients who used the highest cumulative defined daily doses of statins. However, the study had some limitations such as the possibility of miscoding during data acquisition and lack of data on patients' nutritional status, functional conditions, personal habits, and biochemical data. Despite these limitations, the findings suggest that statin use may lower the risk of HFX in T2DM patients and contribute to the literature for future investigations. Lee TC, Chen JC, Lin SY *et al.* **Statin use in patients with type 2 diabetes has lower risk of hip fractures: A Taiwan national population-based study.** *Diabetes/metabolism research and reviews* 2022:e3603. <http://www.ncbi.nlm.nih.gov/pubmed/?term=36579718>

### **Management of paediatric dyslipidemia – updated review**

The article reviews the current and potential future treatment options for dyslipidemia in children. The authors emphasize the importance of early management of dyslipidemia as it has a significant impact on cardiovascular disease risk in adulthood. Currently, statins are the main treatment option for dyslipidemia in children as per guidelines, however, these guidelines are considered outdated as new evidence and treatment options have become available. Despite the availability of well-tolerated and efficacious treatment options, many children with hypercholesterolemia are still underdiagnosed, untreated, or undertreated. The authors suggest that revision of pediatric dyslipidemia guidelines to incorporate newer treatment options and increase awareness among healthcare providers is necessary. The authors also highlight the need for studies specific to children to widen the range of available treatment options for dyslipidemia. Moreover, there is a lack of data and treatment options for children with hypertriglyceridemia, and more studies are needed in this area. In conclusion, the authors emphasize the need for continued research and therapeutic advances in pediatric dyslipidemia management.

Bansal N, Kumar S, Brar PC. **Update on management of paediatric dyslipidaemia.** *Current opinion in endocrinology, diabetes, and obesity* 2023; 30:52-64. <http://www.ncbi.nlm.nih.gov/pubmed/?term=36541082>

### **Increase in ALT at baseline, in statin users, does not predict acute hepatic injury**

The study aimed to evaluate the risk of severe acute liver injury (SALI) in statin initiators with elevated alanine aminotransferase (ALT) levels compared to those with normal ALT levels and non-statin users with elevated ALT levels. The study was conducted using claims data from two large datasets, Optum and MarketScan. Statin initiators with elevated ALT

levels were compared to those with normal ALT levels and non-statin users with elevated ALT levels using propensity score (PS) matching and hazard ratios (HRs) were estimated using proportional hazards regression. The study found that statin initiation was not associated with a significantly higher risk of SALI, regardless of baseline ALT levels. The incidence rate of SALI was about 19/100,000 person-years among statin initiators. The results of the study suggest that baseline ALT status is not a reliable indicator for increased risk of SALI for patients initiating statin therapy. The study was funded by AstraZeneca, the maker of rosuvastatin, but the study analyzed statins as a class of drugs. The study has some limitations, including potential confounding factors not being fully captured in the claims data, outcome and exposure misclassification, and the study being sponsored by AstraZeneca.

Verma SK, Huang J, Hutchinson HG *et al.* **Statin Use and Severe Acute Liver Injury Among Patients with Elevated Alanine Aminotransferase.** *Clinical epidemiology* 2022; 14:1535-1545. <http://www.ncbi.nlm.nih.gov/pubmed/?term=36540900>

## Reduced mortality observed in cerebral hemorrhage patients using statins

The study aimed to examine the relationship between statin use during hospitalization and mortality in patients with intracerebral haemorrhage (ICH). The study was conducted retrospectively using a propensity-matched cohort design and included 1043 patients admitted to the Beth Israel Deaconess Medical Center between 2001 and 2012. The primary outcome was 90-day mortality, which was measured using multivariable Cox regression analysis and propensity score analysis. The results showed that statin use was associated with a 29% lower 90-day mortality rate in patients with ICH. The results were robust in subgroup analyses and propensity score matching and remained stable in sensitivity analysis. The mechanisms of statin use and ICH mortality reduction are unclear, but it may be related to statins' ability to reduce blood lipids and inflammation, improve endothelial function and cerebral blood flow, and inhibit the occurrence of epilepsy. There are limitations to the study, such as the potential for residual confounding factors and the inability to identify the specific aetiology of ICH, obtain data on the dose of statins, and record the cause of death. Overall, the findings suggest that statin use may be associated with lower mortality in patients with ICH, which warrants further investigation.

Yuan M, Zhou X, Lu X *et al.* **Association between statin use during hospitalisation and mortality in patients with intracerebral haemorrhage: a propensity score-matched cohort study.** *BMJ Open* 2022; 12:e065849. <http://www.ncbi.nlm.nih.gov/pubmed/?term=36585154>

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## Relevant Publications

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