



Update week 13 & 14 - 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. **The impact of updated ESC guidelines on lipid management**
 2. **Lipid management in women; improvement needed**
 3. **The connection of coronary calcium and inflammation in statin users**
 4. **Intensive lipid control is pivotal in Korean PAD patients**
 5. **Benefits of statins in CLD patients, a indepth review**
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Comparing the impact of the recent 3 ESC lipid management guidelines

The European Society of Cardiology Lipid Management guidelines has been updated in 2016, 2019, and 2021. To explore the impact of these changes on statin eligibility in primary prevention and LDL-c targets in secondary prevention, the e-Paris registry was queried. This single hospital prospective registry included all consecutive individuals (N=2757) admitted for an ST-segment elevation myocardial infarction (STEMI) at the University Hospital of Pitié-Salpêtrière, Paris, France (2000 – 2018). Eligibility for statins increased from 23.6%, 38.7% and 61.8% from 2016, 2019 and 2021 (p<0.01). Similar findings were observed for men

(62.3% vs 35.0% vs 24.9%, p<0.01) and women (60.2% vs 50.7% vs. 19.3%, p=0.18). the secondary prevention LDL-c goal of <55 mg/dl was reached in 27% of the patients. Almost two-thirds of the patients (61.7%) were eligible for higher statin dosages. Ezetimibe appropriateness in 26.2%, and PCSK9i would have been needed in 12.1% of the participants. For the latter, a greater percentage would be suitable for this therapy in the 2021 recommendations (44.5%) vs. the 2016 guidelines (22.5%; p<0.01). These findings underline the improved guideline recommendations for early detection and management in primary prevention as well as the insufficient LDL-c management in secondary prevention; 70% of

the patients were unable to reach an LDL-c < 50 mg/dl. Increasing statin dosage and adding ezetimibe were the most frequently recommended therapeutic actions.

Sulman D, Zeitouni M, Silvain J *et al.* ESC/EAS Guidelines for the detection, prevention, and treatment of individuals at risk of a first myocardial infarction: effect of 5 years of updates and the new SCORE2. European heart journal. Cardiovascular pharmacotherapy 2022. <http://www.ncbi.nlm.nih.gov/pubmed/?term=35381063>

Lipid management in women – step up the efforts

This review highlights the challenges of cardiovascular risk management in women. Current guidelines have not addressed the specific needs for optimal lipid management in women. A lack of women-focused research is partly to blame. Lipids change during a woman's life due to regular hormonal changes throughout a woman's life cycle, during adolescence, pre-pregnancy, pregnancy, pre-and perimenopause, menopause, and old ages. The authors focus on primary prevention management, highlighting sex-specific risk factors for phase. The use of statins and side effects that could prompt non-statin therapies remain at the forefront of reducing CVD risk in women. Bias regarding aggressive lipid management in women remains a critical hurdle that clinician needs to be aware of. The joined efforts to reach personalized LDL-c goals are quintessential to improving the current inertia observed universally and result in less favorable outcomes in high-risk women compared to men. To increase understanding of the sex-specific differences in lipid management trials and need to emphasize the inclusion of more women.

Sharma J, McAlister J, Aggarwal NR *et al.* Evaluation and management of blood lipids through a woman's life cycle. Am J Prev Cardiol 2022; 10:100333. <http://www.ncbi.nlm.nih.gov/pubmed/?term=35345879>

Statins coronary calcium and inflammation

Coronary calcifications are a marker of atherosclerosis and are associated with an increased risk of complications. Paradoxically statin use is associated with an increase in coronary calcium as well. Although there is an ongoing debate if statin-associated calcifications carry the same risk as naïve calcium deposits, the current understanding of these vascular changes in statin users is limited. In this sub-analysis of the Risk Stratification with Image Guidance of HMG CoA Reductase Inhibitor Therapy (RIGHT) study, the effects of inflammation on coronary calcifications in statin users were evaluated. Participants (N=142) had a cardiac computed tomography angiography (CCTA) at baseline and a 2-year follow-up. Patients were categorized by baseline median hs-CRP levels. Patient with a high baseline median hs-CRP level had an increased BMI: 29 (27–31) vs. 27 (24–28; p < .001), hypertension: 59% vs. 41% (p = .03), and LDL-C levels: 97 (77–113) vs. 87 (75–97; p = .01) mg/dl. After two years of statin treatment, patients with a high baseline media hs-CRP significantly increased dense-calcified coronary burden compared to patients with a low hs-CRP, 1.27 vs. 0.32mm² (p = .02). No differences in non-calcified blockages were observed. The authors suggested that statins act as plaque stabilizing agents, and the observed increase in calcifications reflects plaque stabilizing changes. Patients with at baseline increased hs-CRP, as a surrogate for vascular inflammation, could have more local plaque inflammation and elevated plaque lipid content and subsequently derive more benefit from statin therapy. The observational, retrospective design and small sample size are limitations that need to be addressed in future research to explore these intriguing findings in greater detail.

Scott C, Lateef SS, Hong CG *et al.* Inflammation, coronary plaque progression, and statin use: A secondary analysis of the Risk Stratification with Image Guidance of HMG CoA Reductase Inhibitor Therapy (RIGHT) study. Clin Cardiol 2022. <http://www.ncbi.nlm.nih.gov/pubmed/?term=35366378>

Review on statins and chronic liver disease

When statins were introduced, safety concerns included hepatic harm based on the observed elevations of ALT and AST in clinical trials. Recently the notion of hepatic safety issues has been reversed, and statins are now considered potential hepatic protective drugs. In this detailed review, both basic pathophysiological concepts, evidence from pre-

clinical-, retrospective observational studies, and (small) randomized controlled trials are presented. Low-quality evidence supports the notion that statins reduce chronic liver disease (CLD) mortality; moderate-quality evidence suggests that statins reduce the risk of hepatic decompensation, variceal bleeding, and mortality, especially among patients with compensated cirrhosis. Noteworthy is the observation that statin use was associated with a reduced risk of primary hepatocellular carcinoma. Statins are globally one of the most commonly used and available drugs. They are affordable and have an excellent safety profile supporting the rationale to use statins in patients with CLD. In the context of an exponentially increased incidence of NAFLD; associated with major CVD risk factors and an increased risk of ASCVD complications, statins are attractive to improve the outcomes of both progressive chronic disorders. As such, additional large prospective interventional RCTs are urgently needed to better evaluate the association between statin exposure and the risk of CLD. progressionKreidieh M, Hamadi R, Alsheikh M *et al.* **Statin Use in Patients With Chronic Liver Disease and Cirrhosis: Current Evidence and Future Directions.** *Gastroenterology research* 2022; 15:1-12. <http://www.ncbi.nlm.nih.gov/pubmed/?term=35369681>

Impact of high intensity statins on MACE and MALE in Korean PAD patients

Patients diagnosed with peripheral artery disease (PAD) are categorized as very high risk. Despite this universally accepted recommendation, reluctance for aggressive LDL-c management remains common. In Asia, this is enforced by the notion that less potent statins or lower dosages of high-intensity statins are sufficient for adequate lipid management in patients of Asian ethnicity. In this single-center retrospective analysis of 376 Korean patients with lower extremity PAD that underwent endovascular revascularization, the impact of aggressive LDL- management was evaluated. Patients were grouped into no-statin, low-to-moderate statin users (LMI), and high-intensity statin users (HI). The primary outcomes were major adverse cardiovascular events (MACE) and major adverse limb events (MALE). After a median follow-up period of 40 months, the incidence of MACE in the no-statin, LMI, and HI was 11.4% vs. 16.0% vs. 39% ($p<0.001$), respectively. The lowest incidence of MACE and MALE was observed in the HI group, HR: 0.447(0.244–0.834; $p=0.018$) and HR: 0.360 (0.129–1.006; $p=0.051$), respectively. Patients in the LMI group had fewer MACE than no-statin users, HR: 0.571 (0.326–1.0; $p=0.050$). The HI group had better MALE outcomes compared to the LMI patients, HR: 0.432 (0.223–0.837; $p=0.003$). The authors concluded that HI and LMI statin use is associated with a significant reduction in MACE events compared to no-statin use. HI statin use was associated with better MALE outcomes than no-statin or LMI statin use.

Kim GS, Seo J, Kim BG *et al.* **Impact of Statin Treatment Intensity after Endovascular Revascularization on Lower Extremity Peripheral Artery Disease.** *Yonsei medical journal* 2022; 63:333-341. <http://www.ncbi.nlm.nih.gov/pubmed/?term=35352884>

Relevant Publications

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