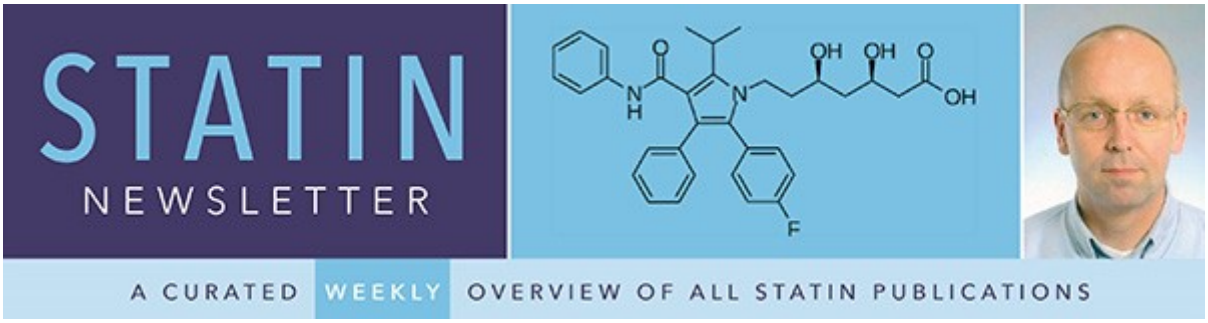

Update week 45 & 46 - 2023

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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Key Publications

1. **Diabetes risk of statins; a meta-analysis.I**
2. **Should patients with chronic liver disease use statins?**
3. **Impact of statins in patients with embolic stroke of undermined origin**

Key publications

Meta analysis on statin related diabetes risk in primary prevention

This updated meta-analysis, which includes data from eight studies encompassing 70,453 patients, aims to unravel the association between statin use and the onset of new diabetes, particularly in a primary prevention setting. The study's unique approach lies in its stratification of participants based on their baseline diabetes risk, delineating into two groups: those with low (< 7.5 events per 1000 patient-years) and high (≥ 7.5 events per 1000 patient-years) baseline rates of diabetes. The meta-analysis reveals a globally increased risk of new-onset diabetes in patients undergoing statin therapy (Odds Ratio [OR] 1.1), aligning with previous literature indicating a marginal but notable risk elevation. Notably, this risk amplification becomes more pronounced (OR 1.2) in the subset of studies featuring patients with a higher baseline risk of diabetes, underscoring the critical influence of baseline diabetes risk on statin-related diabetes onset. While the findings are compelling, they must be weighed against the backdrop of the study's limitations. The categorization of studies based on event rates, rather than individual patient data, and the arbitrary selection of the cut-off point for defining "low" or "high" risk groups, might have influenced the results. Additionally, the inherent clinical heterogeneity among the included studies, as well as variations in the definition of new-onset diabetes, introduces potential confounding factors. The study's conclusions emphasize the nuanced relationship between statin therapy and diabetes risk, suggesting that the risk of new-onset diabetes is more dependent on patient characteristics rather than the specific type of statin. However, it is imperative to note that the overall risk increase is relatively modest compared to the substantial cardiovascular benefits conferred by statins. Future research should aim to refine these findings and explore strategies to mitigate diabetes risk in susceptible populations while leveraging the cardioprotective effects of statins. In summary, Masson et al.'s research contributes to a growing body of evidence highlighting the need for personalized medicine approaches in statin therapy, these findings suggest that population characteristics are more important than the type of statin used to explain the association. Considering some limitations of this study, the results should be confirmed.

in future research.Statins and new-onset diabetes in primary prevention setting: an updated meta-analysis stratified by baseline diabetes risk. Acta diabetologica 2023; Masson W, Lobo M, Barbagelata L, Nogueira JP. http://www.ncbi.nlm.nih.gov/pubmed/?term=37934231

The role of statins in patients with chronic liver disease - review

This article provides a comprehensive overview of the emerging role of statins in the management of chronic liver disease (CLD) and cirrhosis. The authors rightly highlight the non-traditional benefits of statins beyond their well-established cardiovascular effects. These benefits include anti-inflammatory, anti-fibrotic, vasoprotective, and antioxidant effects, which are potentially useful in mitigating complications of CLD. The molecular basis for these pleiotropic effects, involving the modulation of pathways like Rho and Ras proteins and the nitric oxide pathway, is well-explained and substantiates the theoretical rationale for using statins in this context. However, the article also acknowledges the paucity of large-scale, randomized controlled trials (RCTs) directly addressing the impact of statins on patient-important outcomes in CLD and cirrhosis, such as decompensation rates, hepatocellular carcinoma incidence, and overall mortality. The studies referenced are predominantly observational or small-scale RCTs, which, while promising, do not provide conclusive evidence.

The safety profile of statins in cirrhosis, especially in advanced stages, is a critical aspect of the discussion. The article effectively addresses concerns over statin-associated hepatotoxicity and muscle toxicity, including rhabdomyolysis, particularly in patients with decompensated cirrhosis. It suggests caution in prescribing statins to this group, advocating for the use of the lowest effective dose and immediate discontinuation in case of severe adverse effects. This recommendation is prudent, considering the potential risks in this vulnerable population.

Future research directions proposed in the article are appropriate and necessary. There is a clear need for larger, more definitive RCTs to assess the true clinical benefits and safety of statins in CLD and cirrhosis. Such studies should focus on a variety of patient-important outcomes, including liver-related and non-liver-related mortality, and explore different statin formulations, doses, and durations. In summary, the article presents a balanced view of the

current state of knowledge regarding the use of statins in cirrhosis. It highlights the potential benefits while acknowledging the limitations and risks associated with their use in this context. The call for further research is well-founded and essential for advancing our understanding and improving patient care in this field.
Statins in Cirrhosis: Hope or Hype? J Clin Exp Hepatol 2023; 13:1032-1046Shaffer LR, Mahmud N. http://www.ncbi.nlm.nih.gov/pubmed/?term=37975036

Statins in patients with embolic stroke of undetermined source (ESUS)

The study employed a longitudinal cohort design, focusing on patients diagnosed with ESUS. The inclusion of comprehensive data on statin therapy—encompassing treatment initiation, dosage, and pre-stroke use—strengthens the study's methodology. The long-term follow-up period of 48 months is commendable, as it allows for a thorough observation of long-term outcomes. However, the study's single-center nature raises questions about the generalizability of the findings. Additionally, the lack of randomization and potential referral bias due to the study's setting in a tertiary hospital could influence the results. The study's findings suggest a significant benefit of statin therapy in reducing the risk of stroke recurrence, major cardiovascular events, and death in ESUS patients. The observed odds ratios indicate a robust association between statin therapy and reduced risk of these adverse outcomes. The early initiation of statin therapy post-stroke appears particularly effective, aligning with existing literature on acute stroke management. However, the study's findings on functional outcomes, while promising, are less conclusive and warrant further investigation. From a critical standpoint, the study fills a crucial gap in stroke research, specifically addressing the effectiveness of statins in ESUS patients—a subgroup often underrepresented in stroke research. The study's focus on both primary and secondary outcomes provides a comprehensive understanding of the potential benefits of statin therapy in this population. However, the study's limitations, including its non-randomized design and single-center scope, must be acknowledged. These factors may limit the applicability of the findings to broader populations and settings.The study's results suggest that statins should be considered a key component of secondary prevention strategies in ESUS patients, especially when initiated early and at higher dosages. This could lead to a paradigm shift in managing ESUS, emphasizing the role of statins alongside other preventive measures. However, clinicians should exercise caution in extrapolating these findings to all ESUS patients, considering individual patient characteristics and the study's limitations. In conclusion, this study provides valuable insights into the role of statins in managing ESUS, a stroke subtype with unique challenges. The findings suggest a potential benefit of statin therapy in reducing stroke recurrence and improving outcomes in ESUS patients. However, further research, ideally involving randomized clinical trials and multicenter studies, is necessary to confirm these findings and establish definitive treatment guidelines for this patient population.
Effectiveness of statins on outcomes of patients with Embolic Stroke of Undetermined Source (ESUS). Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association 2023; 33:107469Vitturi BK, Gagliardi RJ. http://www.ncbi.nlm.nih.gov/pubmed/?term=37944282

Relevant Publications

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