



Update week 23 & 24 - 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. Why inhibition of cholesterol absorption is pivotal
2. Dementia risk in AF patients on OAC and statins
3. Reduction of stroke risk observed in AF patients on statins
4. EVAR patients benefit when using statin
5. Increased ASCVD risk in inflammatory myopathy patients

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## Have we neglected the impact of cholesterol absorption on CVD risk?

This article provides a thorough review on cholesterol absorption and its relation to atherosclerotic cardiovascular diseases (ASCVDs). The authors correctly acknowledge the well-established fact that reducing low-density lipoprotein cholesterol (LDL-C) concentrations aids in lowering the risk of ASCVDs. However, they are proposing that the broader aspects of cholesterol metabolism, particularly high cholesterol absorption, could be a potential risk and challenge the traditional focus on LDL-C alone. A convincing case is presented, based on genetic, metabolic, population-based studies, and lipid-lowering interventions. They highlight the role of intestinal sterol transporters like ABCG5, ABCG8, and NPC1L1 in cholesterol metabolism. This exploration of the genetic factors involved in cholesterol metabolism and absorption introduces a fresh perspective to the understanding of ASCVD risk. The article also re-evaluates the efficacy of statin monotherapy, suggesting that it is insufficient to reduce ASCVD risk in those with high cholesterol absorption. Theoretically one-third of patients with high cholesterol absorption could benefit from a combination therapy of statin with cholesterol absorption inhibition. What remains unaddressed by the authors are the practical implications of such an approach, including potential side effects and costs. A minor weakness is the paper's occasional reliance on data from the Scandinavian Simvastatin Survival Study, which could limit the applicability of the findings to a broader demographic. Future studies could aim to include more diverse populations. The authors conclude that high cholesterol absorption contributes to atherosclerosis and propose combination lipid-lowering therapy and dietary means to reduce cholesterol absorption. Overall, the review is well-structured and insightful, enriching our understanding of cholesterol metabolism's role in cardiovascular diseases. However, more studies are required to definitively recommend changes to the current LDL-C-focused therapeutic approach.

### High cholesterol absorption: A risk factor of atherosclerotic cardiovascular diseases?

*Atherosclerosis* 2023; 376:53-62 Simonen P, Öörni K, Sinisalo J *et al.*

<http://www.ncbi.nlm.nih.gov/pubmed/?term=37290267>

## Risk of Dementia in AF patients receiving OAC and treated with statins.

What is the impact of statin therapy on the risk of dementia in patients with atrial fibrillation (AF) receiving oral anticoagulant (OAC)? The authors make the assertion that statin therapy lowers dementia risk in a dose-dependent manner. This is an observational and retrospective analysis, sourced from the Korean National Health Insurance Service database, and employs a significant population sample of 91,018 non-valvular AF (NVAF) patients. The study's strength lies in its large sample size and the use of robust statistical analysis, which reveals a lower dementia risk in the statin therapy group compared to the non-statin therapy group. The identification of a dose-dependent reduction in dementia risk with statin therapy is a notable finding. However, a potential limitation of this study is the lack of randomization and a control group, which might introduce bias and confounding factors that are difficult to account for. While the study makes several attempts to account for potential confounders, there are inherent limitations to a retrospective, observational study. The study acknowledges the lack of control for unmeasured residual biological variables (lipid profile, blood glucose, uric acid, blood pressure, etc.) and social factors (education, economic status, environmental circumstances, etc.), and potential misclassifications in the diagnostic codes used. There was also no evaluation of the impact of different types of statins, off-label, under-dosed, or different types of direct-acting OACs, which limits the generalizability of the results. Furthermore, the results, while statistically significant, showed only a modest reduction in dementia risk. However this is important, as it may have limited clinical significance, and the authors appropriately call for prospective randomized trials to confirm their findings. Overall, this research offers a novel perspective on the potential role of statin therapy in reducing dementia risk among AF patients on OACs. However, further robust, prospective, randomized studies are required to explore this

relationship further and confirm the causality implied in this study.

**Statin therapy reduces dementia risk in atrial fibrillation patients receiving oral anticoagulants.** *European heart journal. Cardiovascular pharmacotherapy* 2023; Kim MH, Yuan SL, Lee KM *et al.* <http://www.ncbi.nlm.nih.gov/pubmed/?term=37291702>

### **Less strokes in AF patients using statins.**

In this second study focusing on atrial fibrillation (AF) patients, statin use showed significant associations with a lower risk of strokes in patients with atrial fibrillation and emphasizing the impact of low-density lipoprotein cholesterol (LDL-C) levels on stroke rates. The retrospective cohort design allows for large-scale data analysis and utilization of real-world evidence. However, it also leaves room for biases and potential confounding factors, which the authors acknowledged. The reliance on administrative databases potentially misses crucial clinical information, like race, smoking habits, frailty, etc. These factors could significantly influence both the use of statins and the stroke rates. The lack of information regarding who met the criteria for statin therapy as per primary prevention guidelines also raises concerns about the generalizability of the findings. Furthermore, the association between statin use, LDL-C levels, and stroke risk was based on single baseline measurements, which may not capture the dynamic nature of these factors and their impacts on stroke risk over time. Longitudinal data collection or repeated measures analysis would have been more robust. The study also suggests an association of statin use with lower stroke rates, independent of LDL-C levels, which points towards additional protective mechanisms of statins beyond lipid-lowering. Despite its limitations, the study provides valuable insights into the potential role of statins in stroke prevention among patients with AF. Further research, preferably randomized controlled trials, will strengthen these findings and facilitate more informed clinical decision-making.

**Statin Use and Stroke Rate in Older Adults With Atrial Fibrillation: A Population-Based Cohort Study.** *J Am Heart Assoc* 2023; 12:e028381 Shweikialrefaee B, Ko DT, Fang J *et al.* <http://www.ncbi.nlm.nih.gov/pubmed/?term=37318025>

### **The effects of statins in EVAR patients,**

Should statins be started in patients with abdominal aortic aneurysms after an endovascular repair procedure? Centered on data collected in this Korean nationwide population-based study the authors discuss the role of statins in endovascular abdominal aortic aneurysm repair (EVAR) in a Korean context. The study offers valuable insights into this underexplored area, with significant implications for improving health outcomes in patients undergoing EVAR.

However, some concerns remain. The study design, being retrospective and based on national health insurance claims data, inherently limits the robustness of the findings. Key factors such as biochemistry and aneurysm anatomy data are absent, potentially skewing the results. Similarly, the missing information on statin dosage, intensity, and compliance can affect the conclusions drawn. The baseline difference in health status between statin users and non-users, despite the use of propensity score matching, could have resulted in selection bias and overestimation of the benefits of statins. Furthermore, the study's findings are limited to Korean patients and cannot be generalized without additional international comparative studies. The disparity in statin persistence between this study and a Taiwanese study adds another layer of complexity, suggesting potential sociocultural influences on medication compliance.

The study's strength lies in its robust analysis of a large sample size, providing evidence for the continuous use of statins pre- and post-EVAR to decrease all-cause and cardiovascular mortality. However, it remains crucial to conduct more granular, prospective, and possibly randomized controlled studies to verify these associations. In the meantime, these findings should be interpreted with caution, considering the limitations, and further research needs to be directed towards optimal statin intensity and LDL-C targets in EVAR patients.

**Role of Statins after Endovascular Repair of Abdominal Aortic Aneurysms: A Nationwide Population-Based Study.** *Journal of clinical medicine* 2023; 12:Oh GC, Lee KY, Choo EH *et al.* <http://www.ncbi.nlm.nih.gov/pubmed/?term=37297931>

### **Do myopathy patients have an increased ASCVD risk?**

This comprehensive study on cardiovascular (CV) risk in idiopathic inflammatory myopathies (IIM) offers valuable insights. The authors observed an increased prevalence of traditional risk factors and subclinical atherosclerosis in IIM patients, which is a critical contribution to existing knowledge. The use of comprehensive methods, such as carotid intima-media thickness, pulse wave velocity, and body composition, enhances the robustness of the results. However, the study's cross-sectional design is limiting as it does not provide insight into the temporal relationship between the variables. Future studies should adopt a longitudinal approach to address this gap. Also, the exclusion of subjects with pre-existing CV conditions might lead to a selection bias, underestimating the actual CV risk in IIM patients. It would be valuable if the study accounted for the potential effect of this bias. The underestimation of CV risk in IIM by SCORE and its modifications is an interesting finding. However, the study suggests that SCORE2 is the most accurate tool without adequately substantiating this claim with comparative data from other risk calculation methods. More comparative studies on various risk calculation tools are necessary. Furthermore, the study acknowledges its limitation due to a small number of patients, particularly in each IIM subtype, which might affect the generalizability of the results. Replication with larger sample sizes is therefore necessary. The paper, nonetheless, has significant implications for IIM patients' management, highlighting the need for CV risk screening and short-term glucocorticoid therapy. However, further research should explore the potential cardioprotective benefits of other medications. In conclusion, while this study adds value to the understanding of CV risk in IIM, the mentioned limitations must be addressed in future research.

**Cardiovascular risk in myositis patients compared to the general population.** Rheumatology (Oxford) 2023; Oreska S, Storkanova H, Kudlicka J *et al.*  
<http://www.ncbi.nlm.nih.gov/pubmed/?term=37279728>

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# Basic Science

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