



Update week 31 & 32 - 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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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. Poly pill in patients with impaired renal function
2. Improve glycemic control but don't forget statins and RASi
3. Lipids and coronary calcifications; it is not only the cholesterol!
4. Patients with impaired renal function and increased Lp(a) - the effects of statins
5. Impressive benefits of OMT in revascularized PAD patients!

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## Safety and efficacy of the poly pill in patients with impaired renal function

Are fixed-dose combination treatments for the primary prevention of cardiovascular disease, for chronic kidney disease (CKD) patients safe and effective? The meta-analysis comprised data from 18,162 participants and focused on those with a low estimated glomerular filtration rate (eGFR), an indicator of kidney function. The results suggest that participants with normal eGFR benefitted from the treatment, witnessing a reduction in the risk of cardiovascular outcomes. However, the benefits were even more pronounced in participants with low eGFR. The combination treatment inclusive of aspirin showed greater relative risk reduction for those with low eGFR than without aspirin. Side effects, with the exception of dizziness, remained consistent across treatment and control groups, and didn't vary significantly based on kidney function. CKD is acknowledged as a global health concern. Individuals with CKD tend to have a higher risk of cardiovascular diseases. Despite this established relationship, past clinical trials often excluded CKD patients. The present meta-analysis bridges this gap by demonstrating that a combination therapy can significantly reduce cardiovascular risks in the CKD population. A few limitations were acknowledged, including varied methods across trials and baseline measurements that may underestimate the actual number of CKD patients. The applicability of results to those with advanced CKD remains uncertain. The Authors concluded that the fixed-dose combination treatment, especially when including aspirin, proves effective and safe for preventing cardiovascular diseases. It's especially beneficial for those with low eGFR, emphasizing its potential role in managing CKD patients at risk for cardiovascular complications.

**Fixed-Dose Combination Therapy for Prevention of Cardiovascular Diseases in CKD: An Individual Participant Data Meta-analysis.** *Clin J Am Soc Nephrol* 2023; Sepanlou SG, Mann JFE, Joseph P *et al.* <http://www.ncbi.nlm.nih.gov/pubmed/?term=37550842>

## Reducing CVD risk in newly diagnosed DM patient warrants statins and RASi

This article explores the relationship between the remission of type 2 diabetes and the risk of cardiovascular events, particularly in newly diagnosed patients. While a previous study demonstrated that remission was linked to a decrease in cardiovascular events among type 2 diabetes patients, there remains a gap in knowledge for those newly diagnosed and identified via routine HbA1c measurements. The Danish guidelines, allowing a 6-month window for lifestyle changes before starting glucose-lowering drug treatment (GLDT), create a unique opportunity to explore this relationship. The study's results indicate that in real-world scenarios, those avoiding initial GLDT showcase a higher 5-year risk of a major adverse cardiovascular event (MACE) compared to those well-managed on GLDT. This higher risk is significant, even in cases of initial remission of type 2 diabetes. Interestingly, those avoiding GLDT also tend to be less treated with risk-modifying agents such as statins and RASi. Prior research corroborated the study's findings of remission being more common shortly after an initial type 2 diabetes diagnosis. However, the link between remission and cardiovascular events remains less explored. The article underscores that in a real-world context, a strategy focused solely on glucose levels may miss significant cardiovascular risk factors. The study also highlights the need for further risk-modifying treatments among individuals bypassing initial GLDT. The implications suggest that more conservative strategies regarding glucose control might impede risk-modifying treatments such as statins and RASi, prompting a discussion on treatment timing in guidelines. While the study benefits from a large dataset and high validity, it acknowledges potential limitations such as unmeasured confounding and the absence of data on certain clinically relevant variables.

**Risk of first-time major cardiovascular event among individuals with newly diagnosed type 2 diabetes: data from Danish registers.** *Diabetologia* 2023; Falkentoft AC, Gerds TA, Zareini B *et al.* <http://www.ncbi.nlm.nih.gov/pubmed/?term=37528178>

## The Effect of Lipids on Coronary Artery Calcification in Young

## Korean Adults

Based on data collected in the KOrea Initiative on Coronary Artery calcification (KOICA) registry, the effects of non-optimal lipid levels on the progression of coronary artery calcification (CAC) in young adults who have never used statins were explored. Using data from 2,940 participants aged 20-45 years from 2002 to 2017, the study specifically aimed to understand the risk of CAC based on different lipid profiles. The key findings were that Only 16.2% of the young adults had optimal lipid levels. Non-optimal lipid levels doubled the risk of CAC progression. The impact was consistent even among those perceived to be at a low risk, such as younger individuals and those with zero initial CAC scores. Surprisingly triglycerides, had the most substantial effect on CAC progression. The aLipid disorders, or dyslipidemia, are a significant predictor of cardiovascular diseases. Although often associated with middle-aged or older individuals, accumulating evidence suggests that prolonged exposure to non-optimal lipid levels from a young age can have detrimental long-term consequences. This is evident from rising dyslipidemia rates among young adults globally. The CAC score is a strong indicator of potential heart disease. The study's results underscore the importance of achieving and maintaining optimal lipid levels from a young age to prevent early onset of CAC and consequent cardiovascular diseases. Despite the focus on LDL-C, the main cholesterol contributor to coronary disease, this study highlights that triglycerides as an equally critical factor for young adults, suggesting a need to revise current screening and management strategies. The limitations of this analysis, based on data collected in the KOICA registry, are that the participants were self-referred young adults who underwent repeated calcium scans. The population-specific behaviors, such as high alcohol consumption and high carbohydrate diet typical in Korea, may also influence the pronounced effect of triglycerides in this cohort. The authors concluded that addressing non-optimal lipid levels, especially triglycerides, is crucial from an early age. Efforts should prioritize early screening, timely interventions, and lifestyle modifications, with a potential focus on dietary changes and reducing alcohol consumption to mitigate CAC progression risks.

**The effect of non-optimal lipids on the progression of coronary artery calcification in statin-naïve young adults: results from KOICA registry.** *Frontiers in cardiovascular medicine* 2023; 10:1173289 Lee H, Ahn HJ, Park HE *et al.* <http://www.ncbi.nlm.nih.gov/pubmed/?term=37534276>

## Lp(a), statins and renal function

The authors of this article explored the relationship between kidney function, statin therapy, and serum levels of lipoprotein(a) [Lp(a)] in Type 2 Diabetes Mellitus (T2DM) patients. High serum Lp(a) levels are correlated with kidney disease in T2DM patients, and recent studies suggest that statins, commonly used to treat high cholesterol, may influence Lp(a) levels. The study involved 149 Japanese patients with T2DM, separated into groups based on statin use. The findings revealed that patients taking statins had higher Lp(a) levels compared to those not on statins. Additionally, there was an inverse correlation between estimated glomerular filtration rate (eGFR) - a measure of kidney function - and Lp(a) in all patients, but this correlation disappeared in statin users. This suggests that high Lp(a) levels are associated with decreased eGFR, but this relationship seems to be attenuated in patients taking statins. The study's implications are significant as they hint that while statins might elevate Lp(a) levels, they could also mask the relationship between Lp(a) and renal function. The limitations of this study include its retrospective nature, the absence of genetic testing, and its small scale, suggesting the need for larger, prospective studies in the future.

**Association of Renal Function and Statin Therapy with Lipoprotein(a) in Patients with Type 2 Diabetes.** *J Atheroscler Thromb* 2023; Hiraishi C, Matsui S, Kojima T *et al.* <http://www.ncbi.nlm.nih.gov/pubmed/?term=37558461>

## PAD patients: “Optimal Medical Therapy a day keeps the doctor away”!

In this single-center cohort study, the authors investigated the impact of optimal medical therapy (OMT) on mortality, major amputation-free survival, and clinically driven target lesion revascularization (CD TLR) among 552 patients with peripheral arterial disease (PAD) undergoing endovascular infrapopliteal revascularization. The OMT was described as a

combination of at least one antiplatelet agent, statin, and either ACE inhibitor or AT-2 antagonist, following existing guideline recommendations. Despite the clear guidelines, only 55.5% of patients were given OMT upon discharge! The study results showed improved survival rates over three years, especially for patients diagnosed with intermittent claudication (IC), compared to those with critical limb ischemia (CLI). Notably, patients receiving OMT exhibited better survival and amputation-free survival trends, but no significant difference was found concerning CD TLR based on OMT presence. This study stresses that there's an underutilization of OMT in patients undergoing these interventions, especially more so for CLI patients, despite indicators suggesting its benefit for overall survival and amputation-free survival. This underuse, also documented in prior research, underscores a gap between evidence-based recommendations and clinical practice. The limitations of the study are its sample size, being a single-center, non-controlled design, and the potential overestimation of effect sizes inherent in such studies. The study calls for more education and awareness about the advantages of OMT for PAD patients.

**Impact of Optimal Medical Therapy on Reintervention and Survival Rates after Endovascular Infrapopliteal Revascularization.** Journal of clinical medicine 2023; 12Wittig T, Pflug T, Schmidt A *et al.* <http://www.ncbi.nlm.nih.gov/pubmed/?term=37568548>

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## Relevant Publications

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3. Risk of Venous Thromboembolism with Statins: Evidence Gathered via a Network Meta-analysis. Balkan medical journal 2023; Birdal O, Saygi M, Doğan R *et al.* <http://www.ncbi.nlm.nih.gov/pubmed/?term=37519020>
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5. New biological therapies for low-density lipoprotein cholesterol. Can J Cardiol 2023; Gill PK, Hegele RA. <http://www.ncbi.nlm.nih.gov/pubmed/?term=37562541>
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9. Fixed-Dose Combination Therapy for Prevention of Cardiovascular Diseases in CKD: An Individual Participant Data Meta-analysis. Clin J Am Soc Nephrol 2023; Sepanlou SG, Mann JFE, Joseph P *et al.* <http://www.ncbi.nlm.nih.gov/pubmed/?term=37550842>
10. Statins and Mortality in COPD: A Methodological Review of Observational Studies. Copd 2023; 20:284-291Sule NO, Suissa S. <http://www.ncbi.nlm.nih.gov/pubmed/?term=37550842>

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## Basic Science

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