

Update week 15 & 16 - 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 <u>all recent statin</u> <u>publications</u>. Based on a curated approach to select relevant articles.

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Key Publications

- 1. Lp(a) a residual risk in statin treated diabetic CVD pateints
- 2. Small dens LDL; why we should care
- 3. Lipid management in elderly patients a review
- 4. Australian consensus on managing youg-adult type 2 diabetic patients
- 5. FH and diabetes what do we know?

Risk associated with elevated Lp(a) in statin treated diabetic CVD patients

The REASSURE-NIRS multi-center registry enrolled consecutive patients with CAD requiring percutaneous coronary intervention (PCI) under the guidance of near-infrared spectroscopy (NIRS)/intravascular ultrasound (IVUS) imaging. A total of 741 patients with CAD participated in this registry between 2015 - 2020. This sub-analysis aimed to determine elevated Lp(a) associated residual risk in diabetic and non-diabetic CVD patients. The endpoint was the scale of lipidic plaque materials in target lesions. At baseline highintensity statin use (p = 0.49) and on-treatment low-density lipoprotein cholesterol (LDL-C) (p = 0.32) and Lp(a) levels (p = 0.09) were comparable in diabetics and non-diabetics. Lp(a) levels were significantly associated with maximum 4-mm lipid-core burden index (maxLCBI4mm) in patients with diabetes (p = 0.01) but not in patients without diabetes (p = 0.96). Multivariate analysis showed that LDL-C levels (p = 0.03) predict maxLCBl4mm in patients without diabetes, but not Lp(a) levels (p = 0.91). Both LDL-C (p = 0.01) and Lp(a) (p = 0.04) levels were independent predictors of maxLCBI4mm in patients with diabetes. Even in patients with diabetes achieving LDL-C <1.8 mmol/L (70 mg/dL), Lp(a) levels remained associated with maxLCBI4mm (p = 0.04). The authors pointed out that diabetic CVD patients with elevated Lp(a) showed were associated with vulnerable plaque features

notwithstanding statin therapy.

Nakamura H, Kataoka Y, Nicholls SJ *et al.* Elevated Lipoprotein(a) as a potential residual risk factor associated with lipid-rich coronary atheroma in patients with type 2 diabetes and coronary artery disease on statin treatment: Insights from the REASSURE-NIRS registry. <u>Atherosclerosis</u> 2022. http://www.ncbi.nlm.nih.gov/pubmed/?term=35450750

Review on small dense LDL particle and CVD risk

With potent LDL-c lowering therapies currently available, the absolute CVD risk reduction remains not very impressive. Examples are the Jupiter Study, where 142 statin-treated patients (50% LDL- Reduction) experienced a primary endpoint vs. 251 patients in the placebo group. Comparable outcomes were noted in the FOURIER trial; 1344 patients using the combination of statin + evolocumab (mean LDL-c 30 mg/dL) experienced a primary event vs. 1563 occurrences in patients using only statins (LDL-c 92 mg/dL). Several metabolic markers have been proposed to explain this so-called residual risk. The differences in LDL particle size and composition have shown a significant relationship with ASCVD risk and atherosclerosis disease progression. An increase in the plasma levels of small dense LDL (sdLDL) particles is associated with elevated ASCVD risk even in patients with low LDL-c concentrations. An abundance of small, dense LDL particles is common in CHDs patients; approximately 30-40% of expressing an abundance of sdLDL. In this review, the authors summarize historical and recent clinical trial evidence related to the importance of small, dense LDL (sdLDL) in predicting CVD risk, treatment response, and clinical outcomes. Superko H, Garrett B, Small Dense LDL: Scientific Background, Clinical Relevance, and Recent Evidence Still a Risk Even with 'Normal' LDL-C Levels. Biomedicines 2022; 10. http://www.ncbi.nlm.nih.gov/pubmed/?term=35453579

How to manage lipids in elderly patients - Review

Should elderly patients receive similar guideline dictated therapies, and should we aim for similar LDL-c goals as in younger adult individuals? This review presents a growing body of evidence on why elderly patients could benefit from intensive lipid management strategies. Whether to start or intensify pharmacological therapies in elderly patients deserves particular attention. Factors such as anticipated lifespan, comorbid conditions, physical and cognitive function, independence, polypharmacy, and personal preferences informing risk-benefit trade-offs are essential. Healthy lifestyle choices are considered the basis of CVD risk reduction; however, currently available statin and non-statin lipid-lowering medications can provide additional benefits. The authors review the available evidence on the broad portfolio of lipid-modifying interventions both in secondary and primary prevention settings for elderly patients.

Hassen LJ, Scarfone SR, Milks MW. Lipid-Targeted Atherosclerotic Risk Reduction in Older Adults: A Review. <u>Geriatrics (Basel)</u> 2022; 7. http://www.ncbi.nlm.nih.gov/pubmed/? term=35447841

Managing Type 2 Diabetes in young adult – Australian guidelines/consensus statement

The Australian Diabetes Society, together with the Australian Diabetes Educators Association and Australasian Paediatric Endocrine Group, have written the first-ever Australian consensus statement on the management of type 2 diabetes (DM2) in young adults. This consensus statement provides advice on screening, diabetes type, psychological care, lifestyle, glycaemic targets, pharmacological agents, cardiovascular disease risk management, comorbidity assessment, contraception and pregnancy planning, and patient-centered education. Type 2 diabetes that manifests in younger individuals appears to be a more aggressive condition than in older age groups. Earlier assessment and management of risk factors are advocated. Traditional cardiovascular risk calculators are unlikely to be accurate in this age group, and early statin use is recommended, aiming for an LDL-c target of <100 mg/dl. With the rapidly growing number of young adults developing DM2, this Australian consensus statement fills a gap. The need for more rigorous evidence is underlined and should trigger the development of appropriate registries, studies, and trials. Wong J, Ross GP, Zoungas S *et al.* Management of type 2 diabetes in young adults aged 18-30 years: ADS/ADEA/APEG consensus statement. <u>Med J Aust</u> 2022; 216:422-429. http://www.ncbi.nlm.nih.gov/pubmed/?term=35430745

Do FH patients have a reduced risk for developing diabetes

Conflicting evidence on the causal relationship between familial hypercholesterolemia (FH) and the risk of developing diabetes mellitus type 2 (DM2) is confusing for healthcare professionals responsible for managing FH patients. In this elaborate review the authors dissect the current evidence on this observed mitigating effect of elevated cholesterol on the development of DM2. Several observational studies and registries show a reduced incidence of DM in FH families. In contrast the use of statins, that lower LDL-c, are associated with an increased risk of DM2. LDL-c putatively has a damaging effect of the insulin secreting pancreatic Beta-cells. Lifestyle factors that are playing an important role such as healthy diet and decreased body weight, are observed more frequently in FH patients and could be an explanation for these observations as well. Non-statin LDL-c lowering drugs are not prone for new onset diabetes and there are reports of FH families in whom DM2 is present. This review provides an interesting perspective on the different types of evidence put forward to support or refute the FH and DM 2 connection but points that there are knowledge gaps that need to be addressed to fully understand the interplay between glucose and lipid metabolism.

González-Lleó AM, Sánchez-Hernández RM, Boronat M, Wägner AM. Diabetes and Familial Hypercholesterolemia: Interplay between Lipid and Glucose Metabolism. <u>Nutrients</u> 2022; 14. http://www.ncbi.nlm.nih.gov/pubmed/?term=35406116

Relevant Publications

- Escudero-Martínez I, Matusevicius M, Pavia-Nunes A et al. Association of statin pretreatment with baseline stroke severity and outcome in patients with acute ischemic stroke and received reperfusion treatment: An observational study. <u>Int J Stroke</u> 2022:17474930221095965. http://www.ncbi.nlm.nih.gov/pubmed/?term=35403505
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- 4. Kuriya B, Akhtari S, Movahedi M et al. Statin Use for Primary Cardiovascular Disease Prevention is Low in Inflammatory Arthritis. <u>Can J Cardiol</u> 2022. http://www.ncbi.nlm.nih.gov/pubmed/?term=35429590
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Prevention of Cardiovascular Disease in Patients with Type 2 Diabetes Mellitus. <u>Curr</u> <u>Probl Cardiol</u> 2022:101211. http://www.ncbi.nlm.nih.gov/pubmed/?term=35460688

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Basic Science

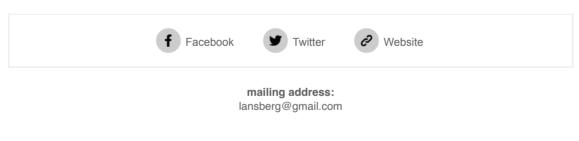
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