

A CURATED WEEKLY OVERVIEW OF ALL STATIN PUBLICATIONS

Update week 03 & 04 - 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 <u>publications</u>. Based on a curated approach to select relevant articles.

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# **Key Publications**

- 1. Predicting ischemic and hemorrhagic strokes in stable CAD
- 2. Polypil for NASH/NAFLD patient reduce to CVD risk
- 3. HOPE-3 should al hypertensive patients use statins?
- 4. Statins show benefit in ESRD patients post PCI
- 5. Statin and ACEi one plus one = three

#### Different risk factors predict IS and ICH in CAD patients

Stable CAD patients are not only at risk for a recurrence but are also prone to develop ischemic or hemorrhagic strokes. This prospective follow-up study included 1428 Taiwanese stable CAD patients using standard medical therapy and were followed for a period of at least 4 years. Based on a multivariate logistic regression analysis, the risk for ischemic stroke was associated with baseline serum levels of myeloperoxidase (MPO), HR:1.89 (1.16-3.10, p=0.01), and statin use, HR:0.37 (0.17-0.79; P=0.01). In contrast with risk for hemorrhagic stroke, which was associated with age, HR:1.07 (1.00-1.14; P=0.04) and ARB use, HR: 0.37 (0.17-0.79; P=0.01), these findings point to possible different mechanisms for developing an ischemic or hemorrhagic stroke and warrant potential different therapeutic approaches to reduce the risk for these cerebral vascular events Prognostic indicators for the onset of ischaemic versus haemorrhagic stroke in stable coronary artery disease. Medicine (Baltimore) 2021; 100:e27973. http://www.ncbi.nlm.nih.gov/pubmed/? term=35049202

#### Reduced their CVD risk in NASH patients using a polypill

NASH is associated with an increased CVD risk, and controlling CV risk factors is relevant

in these patients. This randomized prospective 5-year follow-up study included 2400 NASH patients. NASH was diagnosed using ultrasound and elevated liver enzymes. In the final analysis, 787 patients used the polypill, and 721 were in the control group. The trial endpoints were major CV events (fatal myocardial infarction, sudden death, new-onset heart failure, coronary artery revascularization procedures, fatal and non-fatal stroke, or hospitalization for an acute coronary event); the secondary outcomes were changes in liver function parameters, blood pressure, lipid profiles, and BMI adjusted. MACE risk was 0.35 (0.17-0.73) for participants that used the polypill vs. 0.73 (0.49-1.0) in the control group. Although numerical de events observed were halved inpatient using the polypill, this difference was not statistically significant. The median adherence in the polypill group was 80.4%. High adherence (>70% of provided polypills) was associated with a significantly decreased MACE risk, RR:0.46 (0.30-0.71) when compared to controls and compared to the low adherence group, RR:0.53 (0.33-0.86). For the secondary endpoints of liver function tests participants those with NASH and using the polypill, there was a significant decrease after 60 months of follow-up in patients taking the polypill, an intragroup difference of -12.0 IU/L (-14.2 to -9.6). This is the first report on the use of polypill in patients with NASH/NAFLD. The benefits observed in the Polylran-Liver trial look encouraging and warrant further properly designed randomized trials to confirm these promising findings. Merat S. Jafari E. Radmard AR et al. Polypill for prevention of cardiovascular diseases with focus on non-alcoholic steatohepatitis: the Polylran-Liver trial. Eur Heart J 2022. http://www.ncbi.nlm.nih.gov/pubmed/?term=35048107

# Patients diagnosed with hypertension should use a statin – HOPE-3 trial

revention patients with an annual ASCVD risk of approximately 1% + stage I hypertension. No benefits were observed in patients that used candesartan/HCT + placebo. But patients that used rosuvastatin + placebo or rosuvastatin + candesartan/HCT noted a significant ASCVD risk reduction; HR:0.75 (0.64-0.88; P<0.01) and HR:0.72 ().57-0.89; P<0.003) respectively. The greatest benefits were observed in the patients with the highest tertile of systolic blood pressure. The authors review the available trial data on hypertension control and, combined with the HOPE-3 study data, suggest a standard statin therapy for patients diagnosed with stage II hypertension (systolic blood pressure > 140 mm Hg or diastolic blood pressure > 90 mm Hg) to further reduce their long term ASCVD risk.

McNavish DE, German CA, Shapiro MD. Should a Statin be Given to All Hypertensive Patients? Curr Hypertens Rep 2022; 24:21-27. http://www.ncbi.nlm.nih.gov/pubmed/? term=35072922

#### End stage renal disease patients and statins, the debate continues

Statins failed to show benefit in patients with advanced renal disease on dialysis. The 4D and AURORA trials, using atorvastatin and rosuvastatin, respectively, were both unsuccessful. Despite these findings, the use of statins in patients with advanced renal disease remains under debate. In this PCI registry, 201 chronic hemodialysis patients who had a first PCI were followed for a median period of 2.8 years (0-15.2 years). Patients were divided into 2 groups; with or without statins and with or without high LDL-c (93 mg/dL was used ss cut-off). The primary endpoint was CV death, and secondary endpoints included allcause mortality, non-cardiovascular death, and a 3-point MACE (CV-death, non-fatal myocardial infarction, and stroke). Both Kaplan Meier and multivariate Cox proportional hazard analysis were used to determine the efficacy of satins in this special patient population. Both endpoints were significantly reduced in statin-treated patients. No differences were noted based on median LDL-c levels at time of PCI (P=0.11) Statins were independent predictors for reduced risk of CV death, HR: 0.43 ((0.18-0.88; P=0.02); all-cause death, HR:0.50 (0.29-0.84; P=0.007) and 3P-MmACE, HR:0.50 (0.25-0.93, P=0.03). Despite the limitations associated with the study design, statins used showed promising results in endstage renal disease patients that had a PCI, intriguingly the observed benefits seemed to be unrelated to the LDL-c lowering properties of statins. Patients that used statins were less likely to experience CVD complications

Wang WT, Wu TC, Tseng WK et al

Funamizu T, Iwata H, Chikata Y et al. A Prognostic Merit of Statins in Patients with Chronic

#### Statins and ACEi a dynamic duo

Atherosclerosis starts, progresses, and eventually terminates in (fatal) complications due to endothelial dysfunction. Depending on their severity and duration, CV risk factors interact with endothelial cells to propagate the atherosclerosis process. Two of the most prominent risk factors, hypertension, and dyslipidemia, interact and synergistically accelerate vascular wall pathological changes. Reciprocally managing both risk factors simultaneously will result in greater benefits than simply adding up their individual effects. Both ACEi and statins have shown that their well-recognized CVD benefits reach beyond blood pressure and cholesterol reduction. Both Ang II and NO, critical players in endothelial function, affect oxidative stress, inflammation, and coagulation; both drug classes possess pleiotropic properties that target Ang II and NO and protect the endothelium. This review provides an in-depth overview of the clinical evidence that supports the synergistic benefits of these two drug classes. Statins reduce AT1 receptor expression as well as cholesterol accumulation in macrophages. Both statins and ACEi reduce LDL oxidation, inflammation, matrix degradation in the fibrous cap, smooth muscle cell proliferation/migration, and endothelial dysfunction. An ASCVD fighting duo that is commonly available for an affordable price globally should be part of treatment protocols for most patients with CVD or at risk for **ASCVD** complications.

Borghi C, Levy BI. Synergistic actions between angiotensin-converting enzyme inhibitors and statins in atherosclerosis. <a href="Nutrition">Nutrition</a>, metabolism, and cardiovascular diseases: <a href="NMCD">NMCD</a> 2021. <a href="http://www.ncbi.nlm.nih.gov/pubmed/?term=35082055</a>

## **Relevant Publications**

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- Alsayed N, Almahmeed W, Alnouri F et al. Consensus clinical recommendations for the management of plasma lipid disorders in the Middle East: 2021 update. <u>Atherosclerosis</u> 2022; 343:28-50. http://www.ncbi.nlm.nih.gov/pubmed/? term=35091265
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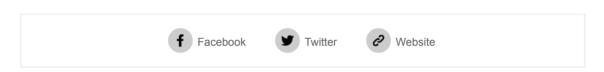
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## **Basic Science**

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