The IAS statin literature update will keep you up-to-date with all recent statin publications, using a curated approach to select relevant articles.

**Key publications**

**Using statins before cardiac surgery reduces renal complications**

Expanding the use of statins in a larger domain of potential benefits is gaining traction. In cardiac surgery, acute kidney injury (CSA-AKI) is associated with increased morbidity and mortality. The exact pathophysiology remains poorly understood, and strategies to reduce this risk are actively explored. The pre-procedural use of statins as a potential prophylactic approach was evaluated in a large prospective study of 58 399 Chinese patients that had cardiac surgery in a single tertiary care hospital between 2012 and 2019. Less renal damage was observed in statin users vs. patients that did not use statins. All stages of CSA-AKI: 30.7% v 36.3% (p < 0.001). Stage 3 CSA-AKI: 0.9% v 2.1%, (p < 0.001). After adjustments for confounding factors, statin use showed an association with a reduced risk for postoperative CSA-AKI, OR: 0.885 (0.852-0.920, p < 0.001) and stage 3 CSA-AKI, OR: 0.671(0.567-0.795, p < 0.001). Using a propensity score-matched analysis, similar outcomes were observed. Preoperative statin was associated with a lower risk of CSA-AKI, 30.7% v 35.3% (p < 0.001).
and stage 3 CSA-AKI, 0.9% vs 2.2% (p < 0.001) than the control cohort. The authors recommend designing a large prospective randomized controlled study to confirm their findings.


**Statins in PAD patient – Meta-analysis**

The benefits of statins in patients with peripheral artery disease (PAD) are stressed in major lipid management guidelines. To date, no placebo-controlled trials to support the use of statins in PAD patients have been published. A meta-analysis was performed to evaluate currently available evidence; a meta-analysis was performed, in which 22 observational cohort studies (N=268 611) were included (1957 – February 2020), including PAD patients and recorded statin use. Outcomes included all-cause mortality (ACM), cardiovascular mortality (CVM), major adverse cardiac events (MACE), and amputation. PAD patients that used statins improved outcomes were observed compared to patients that did not use statins. ACM: OR 0.68 (0.60 – 0.76; NNT=48); HR 0.74 (0.70 - 0.78; (NNT= 10 - 91). MACE, OR 0.84 (0.78 - 0.92; NNT=53); HR 0.78 (0.65 - 0.93) (NNT=167); and amputations: OR 0.59 (0.33 - 1.07; NNT=333); HR 0.74 (0.62 - 0.89; NNT=50). High doses of statins (vs. combined low and moderate doses) were associated with ACM, OR 0.69 (0.43 - 1.09; NNT=17); HR 0.74 (0.62 - 0.89; NNT=16 - 200). for MACE benefits were less robust, OR 0.77 (CI 0.49 - 1.21; NNT=25).

This was also observed for amputations in patients on high doses HR 0.78 (0.69 - 0.90; NNT= 53 - 1 000). Although the quality of evidence was variable, high-dose statins were associated with improved ACM and amputation outcomes. Confirmation by larger trials in PAD patients remain needed to confirm these findings.


**Public knowledge and awareness on cholesterol and cholesterol management remains poor**

One of the major hurdles in CVD prevention is adherence and persistence to medication that address major CV risk factors such as elevated blood pressure and plasma cholesterol. To explore public perceptions of cholesterol and cholesterol management, a nationwide population-based survey was conducted in Singapore. Included were 1000 participants.
belonging to three different ethnic groups, Chinese, Malays, and Indians. The consensus was that cholesterol causes symptoms, and lifestyle improvements would be equally effective as medication to reduce cholesterol (65%). Over half of the participants were convinced that statins cause cancer (56%). One-third of the participants thought that herbal medication/supplements were safer and healthier. Cholesterol-lowering drugs should not be used for more extended periods, and when cholesterol is sufficiently lowered, statins could be stopped, was widely held belief as well (45%). When comparing the three different ethnic groups, Malays were less knowledgeable compared to Chinese, OR: 0.68 (0.47-0.98; P=0.039). Intermediate education compared to primary education was associated with better knowledge, OR:1.67 (1.11-2.51; P=0.013). Overall public awareness and knowledge on cholesterol as an essential CV risk factor and cholesterol management was poor in this multi-ethnic Southeast Asian cohort. Efforts directed at improving this knowledge gap could improve current cholesterol management challenges.


Meta-analysis re-affirms statin benefits in COVID-19 patients

Observational evidence that shows the benefits of statins in patients with COVID-19 is expanding. This recent meta-analysis was based on 25 cohort studies (N=147 824) up to March 2021. In the unadjusted analysis, no benefits were observed, RR:1.16 (0.86-1.57 – 19 studies). After adjustments, statin use did show an association with improved survival, aOR: 0.67 (0.52-0.86 – 11 studies) and aHR: 0.73 (0.58-0.91 – 10 studies). After subgroup analysis, benefits were only noted in patients that used statins for a prolonged period. These outcomes confirm earlier met analyses; however, data from randomized controlled studies must confirm these promising findings.


Depressed, take a statin?

The effects of statins go beyond simple plasma LDL-cholesterol lowering. Benefits are expanding and could include promising new indications not directly related to lipids and CVD risk. When statins were introduced in the early nineties, there were some reports on depression and sleep disturbances related to statin use. Most were case reports, and randomized trials that evaluated statin-related side-effects were unable to confirm these findings. Intriguingly some studies showed not an increase but a decrease in patients that reported symptoms related to depression. In this review and meta-analyses, the authors
explored the major electronic databases, up until April 2021, for studies that evaluated the effects of statins on depression. In total, 72 studies were retrieved. The 15 studies that explored inflammatory-related symptoms of anhedonia, psychomotor retardation, anxiety, and sleep disturbances in depression, and most studies showed an association with statin and improved outcomes. Only a few studies showed no effect, and a minority of the included trials showed some adverse outcomes. This was a narrative report, and no quantitative outcomes were calculated. Based on their findings, the authors concluded that statins are unlikely to cause depressive symptoms in the general population. Promising results indicated a potential role for statins in the treatment of depression. These findings warrant properly designed randomized placebo-controlled trials to confirm that statin could be used to manage depression.


**Relevant publications**

5. Wang L, Cong H, Zhang J et al. Predictive Value of the Triglyceride to High-Density Lipoprotein Cholesterol Ratio for All-Cause Mortality and Cardiovascular Death in Diabetic Patients With Coronary Artery Disease Treated With Statins. *Frontiers in*


This activity is supported by an educational grant from Viatris. © P.J. Lansberg