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**

**Primary prevention – combining a genetic risk score with traditional RF evaluation**

The optimal time to initiate statins in a primary prevention setting has been based on 10-year CVD risk estimates. This strategy does not reflect our current understanding of ASCVD, showing that the magnitude and duration of exposure to elevated LDL-c plasma levels will double our risk for each decade of exposure. Early intervention would result in tripling the benefits of lowering LDL-c compared to initiating treatment later. An alternative approach suggested by the authors is using a genetic risk score as an addition to the traditional risk calculators. This would allow the detection of high-risk individuals early in life and, combined
with the evaluation of traditional risk factors, provide patients with a bespoke type of risk assessment that would allow earlier intervention using statins or alternative approaches to reduce LDL-c and/or additional risk factors. In men, a genetic risk evaluation should be started in their second decade; women could have an evaluation in their thirties or forties. The genetic risk score suggested by the authors has been evaluated in over a million patients of European descent. Current initiatives are ongoing in different countries and ethnic populations, Hispanic, African Americans, and South-Asians. Using this approach would be a momentous paradigm shift from current primary prevention strategies and could improve chances of disease-free survival significantly.


The ongoing saga of statin and hepatic safety in NAFLD

Can statins be used safely in patients with non-alcoholic fatty liver disease (NAFLD), and could statins even benefit NAFLD patients? This meta-analysis combined data collected in 22 studies (16 interventional, 5 cross-sectional, and 1 combined interventional – cross-sectional) that included 2345 NAFLD patients. Hepatic parameters included were ALT, AST, and GGT. Patients that participated in the intervention studies had elevated transaminases, those that received statin therapy had a mean difference (MD) reduction of ALT of -27.2 U/L (-35.25/-19.15) and a percentage reduction of -35.41% (-44.78/-26.04). For AST, an MD of 18.82 U/L (-25.63/-12.02); percentage -31.78% (-41.45/-22.11). Similar reductions were observed for GGT as well, MD of -19.93 U/L (-27.10/-12.77); percentage -25.57% (-35.18/-15.97). The cross-sectional studies showed similar AST and GGT values in patients treated with statins and those without. Based on these findings, statin therapy was not associated with worsening hepatic function in NAFLD patients. Potential benefit was noted in the interventional studies that could point towards a new indication for statin therapy beyond ASCVD risk prevention.


Risk of SAMS; comparing high intensity with moderate intensity statins

To estimate the relative risk of developing statin-associated muscle symptoms (SAMS) based on statin intensity, a meta-analysis was performed on data collected in high-quality randomized clinical trials with >1000 participants and at least two years of treatment. In total, 2919 trials were evaluated, and 24 studies (N=152 146) were included. Outcomes included muscle symptoms (any myalgia and attrition due to muscle symptoms), rhabdomyolysis, and elevated creatine kinase (CK) (>10 x upper limit of normal). Comparing high intensity with moderate intensity
Statins, higher dosing/intensity was associated with increased risk for SAMS. Any muscle problem showed a 4% higher risk, RR 1.04 (1.00 – 1.07; I²=0%). Myalgia, RR=1.04 (1.00 - 1.08; I²=0%), number needed to harm (NNH)=173). Attrition due to muscle problems, RR=1.37 (1.09 - 1.73, I²=0%), NNH=218) and elevated CK, RR=4.69 (2.50 to 8.80; I²=7%), NNH=527. When compared to placebo, the following associations were observed; any muscle problem RR=1.05 (1.01 - 1.09, I²=0%), myalgia (RR=1.13, 95% CI 1.05 to 1.23; I²=0%), NNH=182; attrition due to muscle problems RR=1.55 (1.15 to 2.08, I²=0%), NNH=187 and elevated CK RR=5.37 (2.48 - 11.61; I²=7%), NNH=589. No significant differences were noted when comparing moderate-intensity statins with placebo. The authors estimated that for every 200 patients treated with high-intensity statins, one would experience myalgia or discontinue statin therapy compared with patients using moderate statin therapy.


Statins for primary prevention in elderly Korean patients

Elderly use of statins in primary preventions has not been properly evaluated in a randomized clinical trial and observational; registry data can provide insights into the potentially beneficial and harmful effects. This analysis was based on the Korea Korean National Health Insurance Service-Senior Cohort database (n = 558,147). In total, 81 729 elderly patients (>75 years) with absent signs of symptoms of ASCVD were included in this registry. Those that did not use statins in 2003 were followed from 2004 – 2012. Patients that started with statins (N=3670) were propensity score-matched with patients that did not use statins in a ratio of 1:2. The selected endpoints for this evaluation included myocardial infarction, ischemic stroke, and CVD death. Using a Cox proportional hazard analysis, statins users were significantly better protected than patients who were not using statins. CVD death HR: 0.34 (0.29 to 0.40; p < 0.001). Both diabetic and non-diabetic patients had a reduced CVD mortality. In diabetic patient’s statin use was associated with a reduced risk for MI, HR: 085 (0.55 to 1.33) and ischemic stroke, HR: 0.75 (0.60 to 0.93). This was 0.95 (0.73 to 1.24) and 1.13 (1.01 to 1.26) respectively for patients in whom diabetes was absent. Hypertension was a significant risk factor in the prevention of ischemic stroke by statin treatment as well. The data collected in this large Korean registry confirms early studies showing CVD mortality benefits in elderly patients free of cardiovascular disease that used statins. In diabetic patients, statin use was significantly associated with a reduction of ischemic stroke.

Stopping statins in elderly patients, is there a price to pay?

In elderly patients with multiple co-morbidities, polypharmacy is of great concern. The benefits of statins in septuagenarians are not well established, and stopping statins in elderly or very elderly patients to diminish their “pill burden” is not uncommon. However, the effects of stopping statins have not been adequately studied; In this observational retrospective cohort study, 29,047 Italian patients > 65 years of age and who were treated with statins, blood pressure-lowering drugs, anti-diabetic medication, and antiplatelets from October 2013 – until January 2015, were followed through June 2018. Those that discontinued statins but maintained their other medications during the first 6 months after stopping statins were propensity score-matched (1:1) with patients that continued their medication regimen, including statins. Patients that stopped statins (N=5819) had a mean age of 76.5 (±6.5) years, and 62.9% were men. Of those that stopped, 4010 (68.9%) were matched with those that continued using statins. Those that stopped statins and continued with their other medication were at increased risk to be admitted to a hospital for heart failure complications, HR: 1.24 (1.07 - 1.43); have any cardiovascular outcome, HR: 1.14 (1.03 - 1.26); mortality, HR: 1.15 ((1.02 - 1.30) and have an emergency admission for any cause HR: 1.12 (1.05 – 1.19). However, the observational design prohibits drawing causal conclusions. The outcomes illustrate the potential harm from stopping statins in the elderly with co-morbidities and using a combination of different medications. Benefits were noted in younger and older patients, patients with a mild or severe clinical profile, and irrespective if statins were used in a primary or secondary prevention setting. 


Relevant publications


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### Basic Science publications


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