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**

**Can statins prevent early diabetic nephropathy, a meta-analysis**

Are statins of benefit in patients at risk for renal impairment, or do they cause harmful effects? Using data collected in 9 studies (N=3426), a meta-analysis was performed in patients with early diabetic nephropathy randomized to statins or placebo. The endpoints selected for this evaluation were eGFR, SCR (serum creatinine), hs CRP, TC, and TG. In the studied population, statins were shown to provide renal protection. Compared to the control group patients that used statins had a higher eGFR, mean difference (MD) =5.80 (2.21-9.40; P=0.002) lower SCR, MD =−0.46 (−0.69, −0.24); P<0.0001), lower hsCRP, MD =−1.20 (−2.05, −0.36; P=0.005). Lipid levels were improved significantly as well in the patient’s prescribed statins, TC, MD =−54.09 (−68.02, −40.16; P<0.00001) and TG, MD =−42.19 (−55.54, −28.84; P<0.00001). Despite these promising results, caution is needed. The quality of the included articles was graded as satisfactory; however, the number of trials and participants was very small, and publication bias could not be excluded. However, these findings are intriguing, and properly designed randomized trials are urgently warranted to either confirm or refute these findings.

Which CAC=0 patients can benefit from statins and ASCVD risk factor modification

Are all patients with a calcium score (CAC)=0 at very low risk for ASCVD, or are there subgroups that would still benefit from taking a statin. Using data collected in the MESA (Multi-Ethnic Study of Atherosclerosis) study, 3416 individuals with a CAC=0 and no ASCVD at baseline were selected. Patients were followed for an average period of 16 years. A total of 189 ASCVD events were recorded over this time. CHD events occurred in 91 patients; 88 strokes and 10 patients suffered both. Unadjusted the event rates were low in CAC=0 patients; <5/1000 person-years. This was not different in subgroups of patients with traditional CVD risk factors, except in patients that smoked cigarettes (7.3/1000 person-years), diabetics (8.9/1000 person-years), hypertension (5.4/1000 person-years), and renal impairment (6.8/1000 person-years) Using multivariate-adjusted statistical analysis the following hazard ratio’s (HR) for ASCVD complications were observed, current cigarette smoking, HR=2.12 (1.32–3.42); diabetes, HR=1.68 (1.01–2.80); and hypertension, HR=1.57 (1.06–2.33). The authors concluded that in patients with CAC=0 but who smoked, have diabetes or hypertension, long-term (lifelong) statin therapy, combined with a heart-healthy lifestyle as well as risk factor modification, is warranted.


Sub-analysis of REAL-CAD study, evaluating sd LDL-C

Is LDL-c the ultimate marker to determine the protective ASCVD benefits of statins, or could small dense (sd)LDL-s be superior both in estimating risk as well as predicting benefits? The Randomized Evaluation of Aggressive or Moderate Lipid-Lowering Therapy with Pitavastatin in Coronary Artery Disease (REAL-CAD) study evaluated the benefit of pitavastatin 1 and 4 mg in stable CAD patients. A special automated homogenous assay was used to determine sdLDL at baseline (randomization after a rule-in period, 1 month with 1 mg/d pitavastatin) and after 6 months. Selected (randomly) were 1543 participants who experienced 497 MACE in the REAL-CAD trial. Pitavastatin 4 mg reduced sdLDL-c by 20% more than the 1 mg dosage. IN the patients allocated 1 mg sdLDL-c was associated with increased CAD risk, independent of LDL-c. Comparing the 4th quartile with the 1st quartile resulted in an HR of 1.67 (1.04-2.68, P_interaction=0.001). MACE risk was reduced greater (-46%) in those that used pitavastatin 4 mg vs. those on 1 mg, and in the highest baseline sdLDL-C quartile (>34.3 mg/dL; HR 0.54 (0.36–0.81; p=0.003), but increased relative risk by 40% in patients with 1st quartile (≤ 19.5 mg/dL); HR 1.40 (0.94–2.09; p= 0.099), Risk remained the same for those in 2nd and 3rd quartiles (Pinteraction =0.002). The authors concluded that in the REAL CAAD study that sd LDL-c was predicted ASCVD events independent of LDL-c and that patients with the highest level of sdLDL-c benefitted most from a high dosage of pitavastatin.


Statins a “conditio sine qua non” post CABG

Five large Swedish National registries were merged to evaluate the impact of statins, post coronary artery bypass grafting (CABG), on long-term adverse events. A total of 35 193 patients had a first CABG procedure in Sweden between 2006 and 2017. Survival was > 6 months after CABG before inclusion in the evaluation was executed. The primary endpoint was major adverse cardiovascular events (MACE). Median follow-up time to MACE was 5.3
(interquartile range, 2.5-8.2) years. Most of the patients (95.7%) were prescribed statins after hospital discharge. After 10-years, 78.9% continued using statins. At hospital discharge, 1.4% of patients were prescribed low-, 57.6% intermediate-, and 36.7% high-dose statins. Patients that continued with statins had a significantly lower risk for developing MACE complications. Adjusted hazard ratio aHR 0.56 (0.53-0.59); all-cause mortality, aHR 0.53 (0.50-0.56); cardiovascular death, aHR 0.54 (0.50-0.59); myocardial infarction, aHR, 0.61(0.55-0.69); stroke aHR, 0.66 (0.59-0.73), new revascularization, aHR, 0.79 (0.70-0.88); new angiography, aHR, 0.81 (CI, 0.74-0.88), and dementia, aHR, 0.74 (0.65-0.85). All P<0.01, irrespective of the statin dose. The findings in these large nationwide Swedish registries underline an impressive reduction of important long-term complications post-CABG complications in patients that used statins. The benefits included reductions in mortality, stroke, and dementia. These findings reconfirm the importance of starting and the continued use of statins by very high-risk CVD patients after a CABG procedure.


Can we used CAC to determine risk in HTG patients

Plasma triglycerides (TGs) have re-surfaced as a relevant ASCVD (residual) risk marker; evaluating TG’s as well as managing TG’s is gaining momentum. In this study, the authors determined if coronary artery calcium (CAC) scoring could improve risk stratification for HTG patients in a primary prevention setting. Participants from 4 large registries, the MESA, CARDIA, Dallas Heart Study, and the Heinz Nixdorf Recall study, were re-evaluated, and 2 345 participants with elevated TG’s (150 to <500 mg/dL; or >178-<500 mg/dL if not on a statin) and without clinical ASCVD, were included. Patients were grouped according to CAC scores; CAC = 0; CAC = >0-100 and CAC = >100). The eligibility criteria for icosapent ethyl (IPE) were used as a case example. There was a marked heterogeneity for CAC burden and IPE eligibility; (45% CAC 0; 315 CAC >0-100 and CAC >100). Overall, 17% of participants were eligible for IPE, and 11.9% had ASCVD events within 5 years. Of those participants determined eligible for IPE, 38% had CAC >100, and their event rates were markedly higher (15.9% vs. 7.2%). and the NNT5 2.2-fold lower (29 vs. 64) than those participants with CAC 0. Among the 83% participants not eligible for IPE, 20% had CAC >100, their 5-year incidence of ASCVD (13.9%) was higher than the overall incidence among IPE-eligible participants. The authors suggested that CAC scoring good be a helpful tool for risk stratification and therapeutic decisions. Future trials that aim to evaluate ASCVD risk-reducing interventions in primary prevention HTG patients could use a CAC score >100 cut-offs to facilitate the inclusion of high-risk patients.


Relevant publications


Basic Science publications


