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**

The impact of clinical features on AS characteristics using advanced imaging techniques

Through advanced imaging techniques using optical coherence tomography (OCT) and intravascular ultrasound (IVUS), patients that were scheduled for a coronary intervention were evaluated for plaque burden (IVUS) and lipid, macrophage and calcium indices and the presence of thrombus, plaque rupture as well as thin-cap fibroatheroma (TCFA) by OCT. 704 Japanese patients (44.5% with acute coronary syndromes) were included in this single-center observational study. The median patient age was 66 years, with 81.8% men, 34.4% diabetes mellitus, and 15.5% pre-admission statins. The median lesion length was 25.7 mm, and 33.0% had a TCFA. After Adjustment, relationships between vascular and clinical characteristics showed the following unique features. Age was related to increased calcium deposits but reduced macrophages. Men were more likely to present with more thrombus formation and plaque ruptures, while women had increased thrombus but lacked plaque ruptures. ACS patients demonstrated multiple features associated with vulnerable plaque: more thrombus with and without rupture, more TCFA, lipids, and macrophages + larger
plaque burden. Diabetics had a greater AS plaque burden consisting of lipids, calcium, and more thrombus without rupture. Increased macrophage content was observed in hypertensive patients and current smokers presented with less calcifications. Statin use before admission did not show any impact on IVUS or OCT plaque morphology. The single observation period and the fact that only 15.5% of the patients were using statins (none used high dose, high-intensity statins) could explain this somewhat contradictory finding. The findings of this study show how the different patient characteristics, especially diabetes, age, and sex, impact the underlying atherosclerotic disease progress, affecting the clinical presentation and prioritizing specific risk factor management strategies.


**Statin use associated with increased densification of calcium, but this reflects a decreased AS risk**

The impact of statin use on calcium content and plaque features were evaluated in the PARADIGM study, a large multinational observational registry of patients with clinically indicated serial coronary computed tomography angiography (CCTA). This collaboration consists of 13 sites in 7 countries and collected imaging data of 2252 consecutive CAD patients (2013-2017). This analysis included patients who had serial CCTA at two or more year intervals (N=857). The primary endpoint was a progression of CAD. Patients not using statin showed an increase in all 6 plaque composition types. Statin use was associated with volume decrease in the groups with low attenuation plaques (−30 to 75 HU), β, −0.02 (−0.03 to −0.01; P = .001) and fibro-fatty plaques (76-130 HU), β, −0.03 (−0.04 to −0.02; P < .001). Increased progression of high-density calcium plaques (701-1000 HU), β, 0.02 (0.01-0.03; P < .001) and 1K plaques (>1000 HU), β, 0.02 (0.01-0.03; P < .001). Excluding low attenuation plaques and fibro-fatty plaques at baseline statin use was not associated with changes in overall plaque volume, and calcium dense plaques were associated with attenuated plaque progression. This study shows that statin use was associated with increased densification of calcium of the atherosclerotic coronary arteries, but this reflected not an increase but a diminished atherosclerotic risk.


**Concise review on new developments in lipid management**

For those seeking a compact and concise update on what is new on the lipid management

**Review on Colchicine to reduce residual risk in ASCVD patients**

Inflammation is a critical risk factor for acute ASCVD complications. Despite the unprecedented success of lipid management with statins as monotherapy or combined with other LDL-c lowering drugs, residual risk remains an important factor. New approaches to reduce inflammation targeting IL-1β/IL-6 have been tested and showed promising results but at a premium price. The off-patent anti-inflammatory agent colchicine is an attractive alternative for reducing systemic inflammation and subsequently reducing atherosclerosis progression as well as plaque ruptures. In recent studies, safety and efficacy were examined and showed protective effects without alarming side effects. In secondary prevention patients, several large-scale placebo-controlled randomized trials have been published; the LoDoCo and LoDoCo2 (stable CAD patients), COLCOT, COPS AND CLEAR SYNERGY (recent ACS patients) and the COLCHICINE-PCI trial (post-PCI patients). Based on the evidence by these studies, low-dose colchicine (0.5 mg/day) should be considered in patients with a recent MI (within 30 days and ideally within 3 days) and in stable CAD patients to improve CVD outcomes. Colchicine was well tolerated, and no serious adverse events were observed when combined with high-intensity statins. Patients with severe renal or hepatic function impairment should not take colchicine to prevent toxicity-related adverse events. The benefits of colchicine in diabetics or patients with PAD remain to be established. Marquis-Gravel G, Goodman SG, Anderson TJ et al. Colchicine for Prevention of Atherothrombotic Events in Patients with Coronary Artery Disease: Review and Practical Approach for Clinicians. *Can J Cardiol* 2021. [http://www.ncbi.nlm.nih.gov/pubmed/?term=34418482](http://www.ncbi.nlm.nih.gov/pubmed/?term=34418482)

**Systematic review on cognitive outcomes after traumatic brain injury**

This systematic review explored the potential benefits of statins on reducing the risk of developing dementia in patients that suffered a traumatic brain injury (TBI). This risk increased five-fold compared to individuals that did not experience TBI. Statins have shown some surprising benefits in TBI patients. Of the 4948 studies, 18 were selected for the final
analysis; 9 human studies and 9 animal laboratory trials. Simvastatin was the statin most frequently used in an oral formulation. In four RCTs (N=296), statin use was associated with improved cognitive outcomes. The suggested mechanisms to explain the observed benefits were anti-inflammatory properties, lowering TNF-α and CRP. Additionally, a decrease in axonal injury and cortical thickness changes were observed. Four cohort studies (N=867-953) were evaluated separately, showing reduced mortality in statin-treated patients (P=0.05), a drop in the incidence of Alzheimer’s disease and related dementia’s; RR: 0.77 (0.73-0.81), and in one study, a decreased risk of dementia after concussions (-6.13% (p=0.001). These findings contrasted with one cohort study where statins use was not associated with significantly different outcomes. In the eight animal studies, neuroprotective effects were observed as well. Improved cognitive results and neurological functions showed improvement in statin-treated animals. However, in one animal study, the cognitive abilities showed deterioration. Potential mechanisms suggested were anti-inflammatory effects, stimulated angiogenesis, neurogenesis, neurite outgrowth, proliferation, neural stem cell differentiation, and increased cerebral circulation. The promising results of these studies could promote statins as a therapeutic option for TBI patients. More advanced studies are warranted to confirm the findings, explore optimal dosing, and if statins differ in their capabilities to improve the infaust outcomes in TBI patients.


Relevant publications


Basic Science publications


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