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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

Statins in elderly patients – Real World data

Can statins be safely used in elderly patients, and do they benefit? In this Real World setting of Lombardy (Italy), elderly residents (>65 years) that had ≥ 3 consecutive statin prescriptions (2011-2012) were included in the analysis. The design was a case-control study comparing those deceased in the period 2011-2018 to those that were alive. The mortality risk based on statin adherence was calculated using a logistic regression model. Patients were stratified into four groups (good, medium, poor, and very poor clinical status). The 7-year mortality risk ranged from 11% (good clinical status) to 52% (very poor clinical status). In each of the four categories, statin adherence was associated with a significant reduction of mortality. Adjusted risk for total mortality decreased -56%, -48%, -44% and -47% in the good, medium, poor, and very poor clinical status groups, respectively. For cardiovascular mortality, similar associations were observed. The authors concluded that in a real-world setting, statins adherence was associated with a reduced mortality risk. This was also observed in frail elderly patients; however, the risk reduction was less pronounced compared to elderly in a better physical condition.

Rea F, Mancina G, Corrao G. **Statin treatment reduces the risk of death among elderly frail patients: evidence from a large population-based cohort.** *Eur J Prev Cardiol* 2020.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=33624076>

LDL-c in Japanese ACS patients are inadequately controlled – EXPLORE-J study

The EXPLORE-J study is a 2-year multicentre observational study of hospitalized ACS patients at 59 sites in Japan. In this analysis, lipid-lowering therapy (LLT) and risk of recurrences were evaluated. Data was collected of 1944 patients (mean age 66 years; 80.3% male). Total number of MACE during the 2-year follow-up was 6.2%. CV-death 0.7%; non-fatal ACS 4.5%; stroke 1.7%. Lipid-lowering medication at visit one (V-1) was used by 93.6% (statins), intensive statin 8.2%, and statin + ezetimibe 3.9% of the participants. This increased to 92.3%, 10.5%, and 11.6%, respectively at V-5. LDL-c at baseline (121.3 mg/dL) was reduced to 79.8mg/dL at V-5. The guideline target of an LDL-c <70 mg/dl was reached by 14.4% - 34.6% at V-1 and V-5, respectively. Patients that showed greater LDL-c reduction at V-1 were less likely to experience a MACE, underlining the importance of early LDL-c reduction after ACS. The authors showed that Japanese ACS patients have sub-optimally treated plasma LDL-c levels and suggest that strategies aimed at more intensive LDL-c control are urgently warranted.

Nakamura M, Ako J, Arai H *et al.* Lipid Management and 2-Year Clinical Outcomes in Japanese Patients with Acute Coronary Syndrome: EXPLORE-J. *J Atheroscler Thromb* 2021. <http://www.ncbi.nlm.nih.gov/pubmed/?term=33612707>

Statins use associated with reduced mortality in COVID-19 patients – US, Cerner’s EHR registry

The vascular inflammatory and prothrombotic effects of COVID-19 are frequently found in patients with severe or even fatal outcomes. The repurposing of existing drugs are explored as potential treatments and statins, based on their pleiotropic vascular protective effects, seem to be suited to provide benefits. Data of 117 496 COVID-19 patients from 62 US healthcare centers were collected in the Cerner’s COVID-19 EHR database. Using a propensity score matching based on demographics, comorbidities, and medication indication, statin-treated patients (N = 2,297) were compared to matched controls (N = 4,594). Statin use was associated with a reduced mortality risk of 16.4%; 18.0% of statin-treated patients died vs. 20.6% of those that did not receive statins. The findings are in line with earlier reports that showed statins did not negatively impact outcomes in statin-treated patients and could have an easing effect on disease severity and ultimately mortality. The authors point out that their findings are based on observational findings, and despite their efforts to avoid selection bias, this cannot be ruled in observational studies. They prompt for prospective randomized controlled trials to help define patients more like to benefit from statins therapy to reduce serious or fatal COVID-19 complications.

Marić I, Oskotsky T, Kostić I *et al.* Decreased Mortality Rate Among COVID-19 Patients Prescribed Statins: Data From Electronic Health Records in the US. *Frontiers in medicine* 2021; 8:639804. <http://www.ncbi.nlm.nih.gov/pubmed/?term=33614688>

Effects of statins + RASI on MACE in Korean STEMI vs NSTEMI patients

The Korean AMI Registry (KAMIR) was used to evaluate the impact of statins combined with

renin-angiotensin system inhibitors (RASI) on short- and long-term (2-year) outcomes in STEMI and NSTEMI patients after stent implantation. The KAMIR collected data on 21 890 AMI patients and were treated with statins and RASI. In total 12 490 STEMI patients were compared with 9400 NSTEMI patients; primary endpoints were MACE (all-cause death, recurrent myocardial infarction (Re-MI), and any repeat revascularization). For the final analysis, two propensity score-matched groups were created, each consisting of 5891 STEMI and NSTEMI patients. No significant differences were observed in the cumulative incidences of MACE, re-MI, total repeat revascularizations. All-cause mortality and cardiac death were significantly increased in NSTEMI compared to STEMI patients; HR: 1.407 (1.106–1.790; $p = 0.005$) and HR: 1.311 (1.983–1.749; $p = 0.046$), respectively. The authors concluded that the higher mortality in NSTEMI patients that used statins + RASI is poorly understood but could be related to more STEMI patients who underwent primary PCIA (93.5% vs. 79.2%). Additional studies are warranted to explore the possible mechanisms of the increased mortality risk in NSTEMI patients treated with statins and RASI.

Kim YH, Her AY, Jeong MH *et al.* ST-elevation versus non-ST-elevation myocardial infarction after combined use of statin with renin-angiotensin system inhibitor: Data from the Korea Acute Myocardial Infarction Registry. *Cardiology journal* 2021.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=33634844>

Meta-analysis confirming benefits of lower LDL-c targets

The introduction of effective and safe non-statin treatments has shown that patients achieving lower LDL-c targets are less likely to experience recurrences of ASCVD complications in clinical endpoint studies. National and international guidelines have embraced new targets, reflected by the 2018 AHA/ACC reconditions to aim for an LDL-c < 70 mg/dl for very high-risk secondary prevention patients. This meta-analysis re-evaluated the effects of reaching these lower LDL-c targets compared to patients unable to do so. Eleven randomized controlled trials (N= 130 070) compare intensive vs. less intensive LDL-c management. Median achieved LDL-c was 62 mg/dL in those allocated more intensive, combination therapy vs. 103 mg/dL in patients from the control group. After a median follow-up period of 2 years more intensive LDL-c control, better outcomes for all-cause mortality; absolute risk differences (ARD): -1.56; RR: 0.94 (0.89–1.00)], cardiovascular mortality ARD: -1.49; RR 0.90 (0.81–1.00)], and reduced risk of myocardial infarction, cerebrovascular events, revascularization, and major adverse cardiovascular events (MACE) were noted. Significantly these improvements were not associated with an increased risk for cancer, diabetes mellitus, hemorrhagic stroke. The authors commented that all-cause mortality improvement was observed only in patients who used statins with a baseline LDL-c of ≥ 100 mg/dL. Lower risk of ischemic and safety endpoints was independent of the type of lipid-lowering therapy or baseline LDL-c values.

Khan SU, Khan MU, Virani SS *et al.* Efficacy and safety for the achievement of guideline-recommended lower low-density lipoprotein cholesterol levels: a systematic review and meta-analysis. *Eur J Prev Cardiol* 2020.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=33624058>

Relevant publications

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3. Taha H, Badran HM, Kandil H *et al.* Egyptian practical guidance in lipid management 2020. *The Egyptian heart journal : (EHJ) : official bulletin of the Egyptian Society of Cardiology* 2021; 73:17. <http://www.ncbi.nlm.nih.gov/pubmed/?term=33620601>
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12. Gupta A, Madhavan MV, Poterucha TJ *et al.* Association between antecedent statin use and decreased mortality in hospitalized patients with COVID-19. *Nature communications* 2021; 12:1325. <http://www.ncbi.nlm.nih.gov/pubmed/?term=33637713>

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Basic Science publications

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<http://www.ncbi.nlm.nih.gov/pubmed/?term=33634891>
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