Long-Term Care Updates

August 2021

Statin Deprescribing in the Elderly

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Introduction

Polypharmacy, defined as the chronic use of multiple medications or unnecessary use of medications, is common among older adults. Data from 2002 show that 40% of adults age 65 years or older took 5-9 medications daily, and 18% took 10 or more. Polypharmacy can have negative consequences by increasing the risk of adverse drug events such as side effects and drug-drug interactions.[1] Deprescribing is the process of tapering or stopping inappropriate medications and can minimize polypharmacy and improve patients' health outcomes. Statin use is prevalent among the elderly and ranges from 18% to 45% but has questionable benefit beyond the age of 85 years, so it has been identified as a possible candidate for deprescribing.[2]

This newsletter will explore existing and new evidence on deprescribing statins in the elderly.

Existing Recommendations

There is limited evidence on statin prescribing or deprescribing in older adults who may have complex health problems, as they are often excluded from clinical trials. A systematic review from 2020 evaluated international guidelines on cardiovascular disease prevention with the goal of providing insight on recommendations for statin discontinuation in the elderly. Researchers found 18 relevant guidelines from 11 countries released between 2009 and 2019. In 16 guidelines it was recommended that statins be discontinued due to intolerance, including muscle symptoms, liver dysfunction, and contraindications. However, these recommendations were not exclusively made for older adults. In three guidelines it was suggested that statins may be discontinued due to poor health status, including functional decline, multimorbidity, limited life expectancy, frailty, or if harm outweighs benefit.[2]

The most recent guidelines on cholesterol management from the American College of Cardiology and the American Heart Association were released in 2018, and they include some specific recommendations for older adults. As secondary prevention in patients older than 75 years of age with clinical atherosclerotic cardiovascular disease (ASCVD), it is reasonable to initiate a moderate- or high-intensity statin or continue a high-intensity statin when already tolerated after evaluating the potential for ASCVD risk reduction, adverse effects, drug-drug interactions, patient frailty, and patient preference. As primary prevention in patients older than 75 years of age with diabetes, it is reasonable to continue statin therapy if patients are already tolerating it, and it may be reasonable to initiate statin therapy after discussion between the

patient and physician regarding its risks and benefits. As for deprescribing in adults 75 years of age or older, it may be reasonable to stop statin therapy when functional decline, multimorbidity, frailty, or reduced life expectancy limits its potential benefits.[3]

The Society for Post-Acute and Long-Term Care Medicine released a list titled "Fifteen Things Physicians and Patients Should Question" as part of the American Board of Internal Medicine Foundation's Choosing Wisely campaign which aims to encourage discussion around avoiding unnecessary medical tests and treatments. According to a recommendation last updated in 2015, lipid-lowering medications should not be routinely prescribed in individuals with a limited life expectancy. Studies showed that elderly patients with the lowest cholesterol had the highest mortality and a less favorable risk-benefit ratio when older than 85 years of age.[4]

Limited recommendations exist on statin deprescribing in the elderly, and it is unknown whether this would be beneficial or detrimental to overall patient health, but applying a patient-centered approach that considers the risks and benefits of each individual patient's clinical presentation and preferences appears to be the common recommendation.

New Evidence

Background

While several randomized clinical trials have shown that deprescribing reduces inappropriate medication use, its effects on clinical endpoints, such as hospitalization and mortality, are unclear. Rea et al. recently published a population-based, retrospective cohort study from Italy assessing the clinical implications of discontinuing statin therapy in older patients receiving polypharmacy.[5]

Methods

Clinical outcomes of interest were hospitalization for cerebrovascular disease, heart failure, or ischemic heart disease; emergency department admission for any cause or neurologic disorders; all-cause mortality; the composite of hospitalization for any cardiovascular cause (cerebrovascular disease, heart failure, ischemic heart disease); and the composite of hospitalization for any cardiovascular cause or all-cause mortality. Data were retrieved from the health care utilization databases of Lombardy which included an archive of hospitalizations and outpatient drug prescriptions.

The study design consisted of two steps. In step 1, patients age 65 years or older who were receiving continuous treatment with statins, antihypertensive agents, antidiabetic agents, and antiplatelet agents were first identified, and then among them, those who discontinued statin therapy were later identified. Continuous treatment was defined as a period of 90 days or less between the end of one prescription and the beginning of the next. Patients were followed until all-cause mortality, emigration, statin discontinuation, or the step 1 endpoint date. In step 2, patients from step 1 who discontinued statins but maintained the 3 other therapies for the first 6 months after statin discontinuation were 1:1 propensity score matched to patients who maintained all 4 therapies. Covariates considered during matching were sex, age, comorbidities, adherence to the 4 therapies during step 1, and severity of clinical profile. Patients were followed from 6 months after the date of statin discontinuation until a clinical outcome, emigration, or the step 2 endpoint date.

A Cox proportional hazard model was used to estimate hazard ratios (HR) of the clinical outcomes of interest associated with statin discontinuation. Stratified analyses by sex, age, clinical profile, and whether statins were used as primary or secondary prevention were also performed. Sensitivity analyses were performed to verify the robustness of the main findings. Exposure misclassification could have occurred if patients who discontinued statins resumed them later or patients who maintained

statins interrupted them later, so a Cox proportional hazard model, including exposure to statins during the entire follow up period as a time-dependent covariate, was fitted. Similarly, patients who initially maintained other therapies could have interrupted them later, so the authors censored follow up when another therapy was interrupted. However, doing so could lead to bias by informative censoring, so an inverse probability of censoring weights approach was adopted. Finally, to account for a speculated association between statin discontinuation and clinical outcomes due to confounding by health-seeking behaviors of healthier patients, the authors performed a negative exposure analysis and repeated all the analyses by replacing statins with proton pump inhibitors, a medication expected to be independent of the outcomes studied.

Results

A total of 29,047 patients met criteria for step 1. At baseline the mean age was 76.5 years; 62.9% were men; 1 in 5 had ischemic heart disease; 1 in 12 had cerebrovascular disease, heart failure, and/or respiratory disease; two-thirds of patients had any comorbidity; and more than 10% had a severe clinical profile defined as a Multisource Comorbidity Score of 4 or 5. After an average of 2.4 years of follow-up per patient, 9204 discontinued statins with an incidence of 13.1 events per 100 person-years. Of these 9204 patients, 5819 discontinued statins before other therapies. In step 2, 4023 patients discontinued statins while maintaining the 3 other therapies for the first 6 months after statin discontinuation and were labeled as exposed to statin deprescribing. These patients were older, more likely to be women, and less likely to have heart failure than patients who maintained statin therapy. Ultimately, 4010 of the patients exposed to statin deprescribing were 1:1 propensity score matched to a comparator. After a mean follow up period of approximately 20 months, patients who discontinued statins were more likely to be hospitalized for heart failure (HR 1.24, 95% CI 1.07-1.43) or any cardiovascular cause (HR 1.14, 95% CI 1.03-1.26), be admitted to the emergency department for any cause (HR 1.12, 95% CI 1.05-1.19), experience all-cause mortality (HR 1.15, 95% CI 1.02-1.3), and be hospitalized for any cardiovascular cause or experience all-cause mortality (HR 1.14, 95% CI 1.04-1.24). There was no statistically significant difference between groups for hospitalization for cerebrovascular disease or ischemic heart disease or emergency department admission for neurologic disorders.

Results were consistent whether obtained from the intention-to-treat time-fixed approach or through the sensitivity analyses. Also, there was no evidence from the negative exposure analysis suggesting that proton pump inhibitor discontinuation affected mortality. Stratified analyses did not show evidence that the effect of statin discontinuation was significantly heterogeneous between categories of sex, age, clinical profile, or whether statins were used as primary or secondary prevention.

Discussion

Strengths of the study included a large population, accuracy of data submitted to the prescription database, less potential for confounding by using 1:1 propensity score matching, all-cause mortality as an outcome to avoid uncertainty with diagnostic accuracy, and the consistency of results from the sensitivity analyses, indicating robustness of the main findings.

Limitations of the study included unclear reasoning for statin discontinuation, potential for confounding since allocation was not randomized, adherence derivation from prescription refills which may not correspond to actual use, and exposure misclassification if patients received treatment through private services or made out-of-pocket payments that were not tracked by the database. An attempt to minimize these limitations was made through the sensitivity analyses. Since the study was done in Italy, where the patient population may be more homogeneous, application in the United States may be limited by its diverse population.

The authors concluded discontinuing statins, while maintaining other therapies, was associated with an increased risk of long-term fatal and nonfatal cardiovascular outcomes in elderly patients regardless of age, sex, clinical severity, and whether statins were used as primary or secondary prevention. These results align with previous evidence that lipid-lowering agents

reduce the risk of ASCVD events and statin discontinuation leads to adverse outcomes in high-risk patients like those with acute coronary syndrome, ischemic stroke, or recipients of vascular surgery.

The new evidence provided by this retrospective cohort study supports the continued use of statins in elderly patients who are already taking them.

Conclusion

There are no clear recommendations for deprescribing statins in the elderly. Recent evidence shows that discontinuing statins in the elderly may increase the risk of fatal and nonfatal cardiovascular outcomes which confirms previously established evidence that statins reduce the risk of ASCVD. In elderly patients who are currently tolerating statins, it may be reasonable to continue therapy. Circumstances that would warrant statin deprescribing require further evaluation.

References

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