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REVIEW TOPIC OF THE WEEK

Optimizing Cholesterol Treatment in Patients With Muscle Complaints

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ABSTRACT

Statins are highly effective for preventing cardiovascular events by reducing low-density lipoprotein cholesterol (LDL-C). However, many patients taking statins report muscle-related symptoms that prevent the use of guideline recommended doses. Patients with reported intolerance to statins have a high risk of cardiovascular events. Clinical strategies that optimize cardiovascular risk reduction through LDL-C lowering need to be applied in patients experiencing intolerable side effects that they attribute to statins. In this paper, the authors review definitions of statin intolerance, propose algorithms to better define statin intolerance, and describe approaches to optimize cardiovascular risk reduction among individuals reporting statin-associated muscle symptoms. (J Am Coll Cardiol 2017;70:1290–301)

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Treatment with moderate- and high-intensity statins reduces the risk of atherosclerotic cardiovascular disease (ASCVD) in the setting of high-risk primary and secondary prevention (1,2). For every 1 mmol/l reduction in low-density lipoprotein-cholesterol (LDL-C), ASCVD events are reduced by 21% after 1 year of treatment with moderate- or high-intensity statins (3). The reduction in ASCVD increases with long-term statin use (4).

Randomized clinical trials (RCTs) indicate that statins have a side-effect profile almost indistinguishable from placebo or comparator drugs, particularly when used in low dosages (5,6). However, "real world" data obtained from surveys, registries, and insurance claims suggest that side effects of statins are common, especially at higher doses (7,8). Many patients are unwilling to continue with guideline-recommended statin doses after experiencing side effects (9).

This review presents recommendations from a forum of researchers and clinicians convened to discuss strategies for managing statin intolerance and optimizing LDL-C reduction in patients with muscle complaints. Most statin-associated adverse events are not life-threatening, may or may not be asymptomatic, may or may not cause reductions in medication compliance, and may not reoccur upon rechallenge, even with the same statin (10,11). Therefore, a standardized strategy designed to optimize the continued use of statins in patients who perceive that their muscle symptoms are statin induced may substantially reduce ASCVD events.

CLINICAL CONSEQUENCES AND ECONOMIC COSTS OF NONADHERENCE TO STATINS

Discontinuation or down-titration of statin therapy is associated with an increased risk of future ASCVD events (12,13), resulting in higher health care costs (13). Using the algorithm developed in Medicare beneficiaries (14), patients with statin intolerance versus high statin adherence experienced a higher risk for recurrent myocardial infarction (hazard ratio [HR]: 1.50; 95% confidence interval [CI]: 1.30 to 1.73) and coronary heart disease events (HR: 1.51; 95% CI: 1.34 to 1.70), but no difference in mortality (HR: 0.96; 95% CI: 0.87 to 1.06). An analysis that used an algorithm developed in the Henry Ford Health System (15) reported that patients with statin intolerance had higher health care costs (13).

DEFINITIONS OF STATIN INTOLERANCE

Addressing statin intolerance requires a rigorous approach to verify the problem and concerns about quality of life, while optimizing ASCVD risk reduction (16–19). There is no universally accepted definition of statin intolerance (**Table 1**) but published definitions generally agree on the diagnostic criteria (**Table 2**) (16–19).

All definitions of statin intolerance require dechallenge and rechallenge phases to assess potential causal associations and multiple statin challenges

ABBREVIATIONS AND ACRONYMS

AHA = American Heart Association

ACC = American College of Cardiology

ASCVD = atherosclerotic cardiovascular disease

CI = confidence interval

CK = creatinine kinase

HR = hazard ratio

LDL-C = low-density lipoprotein-cholesterol

RCT = randomized clinical trial

SAMS = statin-associated muscle symptoms

SAMS-CI = Statin-Associated Muscle Symptoms Clinical Index

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