

AIM-LO: LDL-C: Lower for Longer is Better

Presented by Dr. Robert Hegele

Introduction

Hello, I'm Rob Hegele, co-author of the 2021 CCS Dyslipidemia Guidelines. Today, I'm going to talk to you about the role of LDL-cholesterol in atherosclerotic cardiovascular disease, the recent evidence around the impact that lowering LDL-cholesterol has on plaque regression and stability, and also to explain why experts now say: Lowest LDL-Cholesterol for Longer is Better.

The LDL Cholesterol Hypothesis

To start, let's go back to the LDL-cholesterol hypothesis. This is the concept that elevated LDL is a key risk factor, indeed a causal factor, for the development of atherosclerosis and cardiovascular disease.

The cholesterol hypothesis has been around for several decades, and it is founded on several observations. First, cholesterol deposits constitute a significant component of atherosclerotic plaques, and there is strong evidence that the cholesterol ends up in plaques and has been delivered there by LDL particles. Second, reducing LDL levels can result in significant angiographic regression of coronary atherosclerosis. Third, LDL cholesterol-lowering contributes to plaque stabilization. Studies using coronary angiography and intravascular ultrasound showed that high-risk, high-lipid vulnerable plaques were stabilized by lipid-lowering interventions, and this paralleled reductions in LDL-cholesterol levels.

Cholesterol-Years: Taking into account the magnitude and duration of exposure to LDL-C

More recently, observations from these large Mendelian randomization, genetic, studies brought forward the concept of "area under the cholesterol curve".

This is like the concept of "pack-years" of cigarette smoking, except the analogy would be "cholesterol-years" This notion of "cholesterol-years" takes into account the product of the magnitude and duration of exposure to LDL-cholesterol over time to estimate risk of atherosclerotic cardiovascular disease.

For instance, individuals with familial hypercholesterolemia, who from birth have high levels of LDL-cholesterol, have the largest area under the curve at any given age, the steepest slope of LDL-cholesterol versus age, and therefore, when untreated, the earliest onset of ASCVD.

In contrast, there are other individuals, very fortunate genetically, who have low levels, are born with low levels of LDL-cholesterol, or other reasons for low levels, diet or good lifestyle. They have less cumulative exposure and lower risk of developing ASCVD.

Clinically Relevant Implications

The clinically relevant implications are:

- that a measure of exposure to cholesterol over time is superior to a single static measurement of cholesterol at a given time
- and, also, that the long-term risk of cardiovascular events is significantly influenced by LDL levels over the course of a life.

Thus, lower LDL-cholesterol for longer truly is better for reducing the future risk of atherosclerotic cardiovascular disease.