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Heart Disease

Atherosclerotic cardiovascular disease

Atherosclerotic cardiovascular disease (ASCVD) is the most common type of heart disease. It is caused by buildup of plaque inside the walls of coronary arteries. In this newsletter, we will address the lipids and lipoproteins that contribute to ASCVD risk. Of course, they include LDL- and HDL-cholesterol and triglycerides. But they also include subfractions of LDL and HDL. We will focus mainly on these subfractions.

Lipoproteins and cholesterol—brief review

Cholesterol-containing lipoproteins are one of the main things that make up plaque. Cholesterol and other lipids bind to protein to form lipoprotein particles. These are divided into different types based on their size and density. The two most important cholesterol-containing lipoprotein particles are:

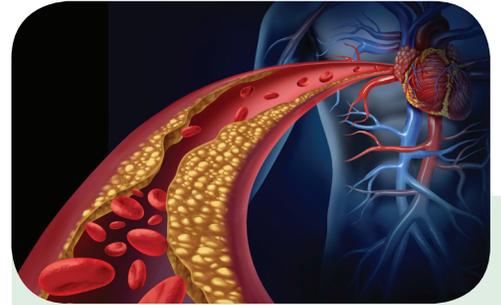
- Low-density lipoprotein (LDL)
- High-density lipoprotein (HDL)

LDL and HDL particles have different roles. LDL carries cholesterol from the liver, where cholesterol is made, to other cells in the body. LDL is the main lipoprotein involved in plaque formation. Cholesterol carried by LDL is called LDL-cholesterol (LDL-C). It is more likely to be deposited into the artery wall. High concentrations of LDL-C are associated with increased risk for ASCVD.

HDL acts as a scavenger. It carries cholesterol from cells in the body back to the liver, where cholesterol is broken down and disposed of. HDL doesn't deposit cholesterol into the walls of blood vessels. So it doesn't contribute to the buildup of plaque. Cholesterol carried by HDL is called HDL-cholesterol (HDL-C). The higher the HDL-C level is, the lower the risk of coronary heart disease.

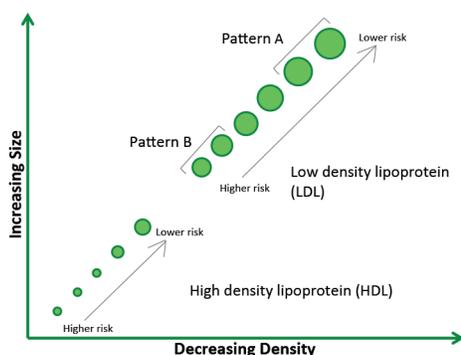
LDL and HDL subfractions

LDL and HDL can be further subdivided into subfractions. Subfractions are based on the size and density of the particles. LDL particles are divided into subfractions ranging from smaller, more dense particles up to larger, less dense particles. HDL particles can be divided into smaller and larger subfractions as well (see Figure). Different people have different amounts of these subfractions.



Heart disease starts in childhood

We know that cardiac events occur in adults. But heart disease actually starts in childhood. When children have high cholesterol levels, plaque begins to form just as it does in adults. So those who have high cholesterol levels during childhood are more likely to have ASCVD in adulthood. This is why the American Academy of Pediatrics (AAP) recommends doing a fasting lipid panel when children are 9 to 11 years old. The AAP also recommends a lipid panel between ages 17 and 21 years. For those between ages 12 and 16, AAP recommends testing only in certain situations. See reference 1 for information.



Clinical relevance of lipoprotein subfractions

Smaller LDL particles are associated with a higher incidence of ASCVD than larger LDL particles.² One reason for this is that small particles can more easily pass from the blood stream into the blood vessel wall, where plaque forms. People with a high level of *small* LDL particles are said to have LDL pattern B. People with a high level of *large* LDL particles have LDL pattern A. Pattern B is associated with a greater risk for heart attack than pattern A.¹

Another important factor is the number of LDL particles (LDL-P). The more LDL particles a person has, the greater the risk of ASCVD.³ This is because a higher number of LDL particles, whether small or large, leads to more plaque formation.

Another important factor related to lipoprotein subfractions is the concentration of HDL particles. Large HDL particles are thought to offer the most protection against ASCVD.^{4,5}

The clinically ideal lipid subfractions are:

- Low concentrations of small and medium LDL
- Pattern A
- Low LDL particle number (LDL-P)
- High concentration of large HDL

Treatment can improve lipoprotein subfraction levels for all of these.

Americans at risk

Total cholesterol and HDL-C are risk factors for ASCVD. A *high* blood level of total cholesterol increases the risk of ASCVD. A *low* level of HDL-C also increases the risk of ASCVD. Here are some other risk factors for ASCVD:

- Gender (men are at greater risk than women)
- Age (risk increases with age)
- Race (African Americans are at greater risk)
- High blood pressure
- Diabetes
- Smoking
- Being overweight or obese
- Diet high in saturated fat and sugar; low in fruit, vegetables, and whole grains
- Physical inactivity

Measuring lipoprotein subfractions

Tests that measure lipid subfractions use a number of different methods. These include:

- Ultracentrifugation
- Nuclear magnetic resonance
- Electrophoresis
- Ion mobility

Most of these methods determine the concentration of some LDL and HDL subfractions in a roundabout way. The ion mobility method is different. It directly measures the size and concentration of all subfractions.⁶

Ion mobility and ASCVD

Ion mobility technology has been used in several clinical studies. One of these showed that a high concentration of small LDL particles was linked to an increased ASCVD risk.⁷ The study showed the same is true for medium LDL particles.⁷ Low levels of large HDL particles were also linked to increased ASCVD.⁷

Two other studies found that people with a high number of LDL particles were at risk for ASCVD.^{8,9} It didn't matter what lipid panel results these people had.

What is the Cardio IQ® Lipoprotein Fractionation Ion Mobility test?

This is a test offered by Quest Diagnostics. As the name implies, it measures lipid subfractions using an ion mobility method. It includes LDL and HDL subfractions, LDL pattern, the total number of LDL particles, and a special interpretive report. It identifies ASCVD risk factors not revealed by a lipid panel. It can be used for people:

- With intermediate risk of ASCVD based on traditional and/or emerging risk factors
- Who have a normal lipid panel and either ASCVD or a high risk for ASCVD
- Being monitored for therapeutic response

References

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