

Healthcare industry BW

Diagnostics

New test for extended blood fat analysis

Cholesterol is seen as the cause of atherosclerosis, a disease that can lead to heart attacks and strokes. However, it now seems that the way cholesterol is packaged may be even more important than high blood cholesterol levels. Nuclear magnetic resonance (NMR) spectroscopy now allows the high-throughput analysis of such lipid packages. MVZ Labor Ravensburg GbR has been offering the measurement of lipoproteins in the blood as part of preventive health examinations since early 2017.



PD Dr. Dietmar Plonné
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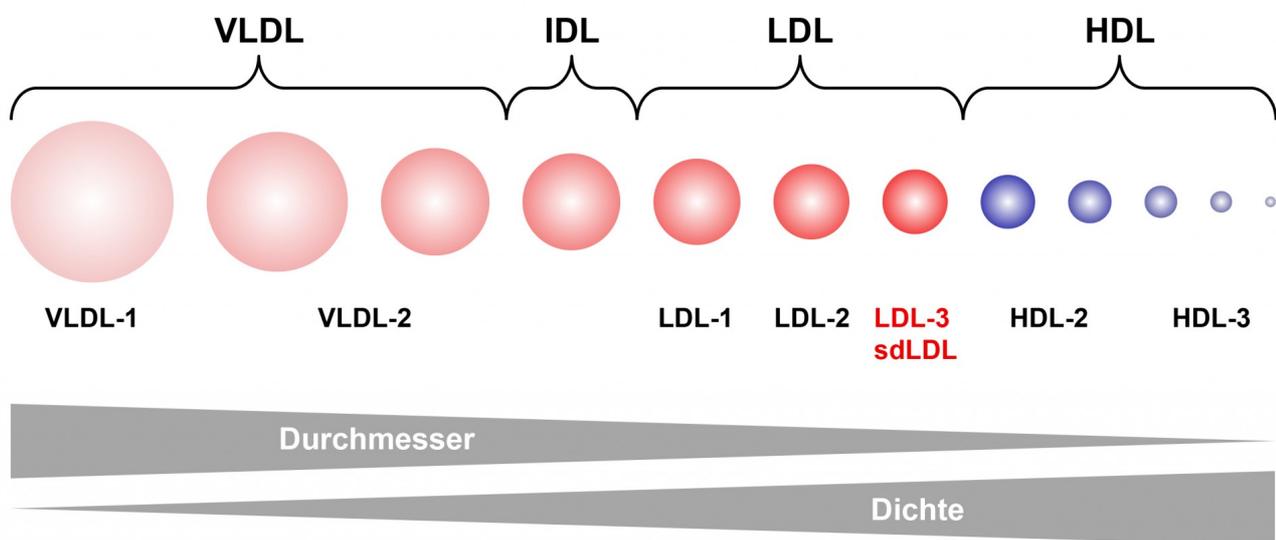
When lipids, including cholesterol, triglycerides and fat-soluble vitamins, are transported in the blood, they are coupled to transport proteins. These fat-protein "packages" are called lipoproteins. Depending on their composition, lipoproteins can be divided into lipoproteins of very low density (VLDL), low density (LDL), high density (HDL) and so-called chylomicrons.

Doctors are mainly focusing on LDL (low density lipoprotein) particles as it is mainly these proteins that transport cholesterol from the liver into the body's cells. In people with elevated LDL levels, LDL attaches to the walls of the blood vessels. This can trigger inflammation that in turn promotes atherosclerosis. In contrast, HDL (high density lipoprotein) particles remove excess cholesterol from the body's cells and transport it back to the liver where it is broken down. High HDL cholesterol levels are therefore thought to provide protection against vascular calcification.

This is why doctors aim to lower elevated

LDL cholesterol levels. However, the simple formula "the lower the LDL cholesterol levels, the lower the risk of heart attacks or strokes" is not always true. The processes leading to atherosclerosis are far too complex to put the risk of heart attacks and strokes down to this one formula. Kidney and diabetes patients with relatively low LDL cholesterol levels are in fact those with the highest risk of heart attacks or strokes. On the other hand, elevated LDL cholesterol levels are not necessarily associated with an increased risk of heart attack/stroke. "Cholesterol is not inherently bad. In fact, it is a vital lipid in the human body," says Dietmar Plonné. The human body produces bile acid, sex hormones and vitamin D from this fat-like substance. In addition, cholesterol is an integral component of the cell membrane.

Enormous variety in lipoproteins – from large and light to small and dense



Schematic representation of the major classes and subclasses of lipoproteins. The density of the particles increases as the particle diameter decreases. Small, dense LDL (sdLDL) particles in the blood promotes atherosclerosis to a much greater extent than bigger, but lighter LDL particles.

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Plonné, managing director and head of laboratory at MVZ Humangenetik Ulm GbR, believes that the total amount of cholesterol in the blood as well as in the LDL and HDL fractions, as measured in routine diagnostics, does not always provide the most meaningful diagnostic solution. In fact, lipoproteins can be further subdivided into particles of different sizes and densities. Studies have shown that it makes a difference if the same amount of cholesterol is distributed across a few large LDL particles or across many small and dense LDL particles (sdLDL). The latter are especially dangerous because they are degraded more slowly and can be transferred into the arterial wall.

Up until 2012, Plonné was responsible for lipoprotein diagnostics at a company that is now called MVZ Labor Ravensburg. It was there that he established density gradient ultracentrifugation as a routine method for advanced lipoprotein diagnostics to assess lipoprotein subgroups.

Ultracentrifugation is still considered the gold standard in lipoprotein diagnostics by which other methods are measured. "It is a great method, but it requires a lot of time and personnel," says Plonné. His laboratory in Ulm only manages to analyse 16 samples a day using a test called

LipoDens®.

The fat metabolism expert therefore went on to look for a method with higher throughput and in 2010 came across an NMR diagnostic company called numares AG in Ravensburg, southern Germany. Back then, the company already owned a patent for a novel NMR-based method that enabled the routine determination of lipoproteins in body fluids. Biophysicists at the company calculate the number and size of the different lipoprotein particles as well as their cholesterol and triglyceride quantities from the NMR signals emitted from the terminal carbon groups of the different lipoprotein particles.

”Ultracentrifugation is no longer necessary”

The companies joined forces and the cooperation proved fruitful for both sides: numares had the technical knowledge and equipment to perform the measurements, and MVZ Labor Ravensburg had the physicians that were able to turn the NMR results into medical findings. Together, the partners have adapted a calculation algorithm for numares’ test so that the results match those of ultracentrifugation as closely as possible. The cooperation partners were looking to address a hitherto unsolved problem: "The term sdLDL is not a uniformly defined category and varies depending on which method is used to analyse the lipoprotein particles," says Plonné. The cooperation partners have been offering this NMR spectroscopy-based test since early 2017. According to the two partners, the test allows them to measure more than 250 samples a day. Plonné now coordinates the expanded lipoprotein diagnoses of the two laboratories from his office in Ulm. Plonné is also one of the lipid metabolism experts within the German Limbach Diagnostic Group, which comprises MVZ Labor Ravensburg and MVZ Humangenetik Ulm.

"In future, it will no longer always be necessary to carry out expensive ultracentrifugations because NMR spectroscopy produces similar results in most cases," says Plonné. "Ultracentrifugation is only necessary for high-fat serum samples of a milky-cloudy consistence, or for samples that contain atypical lipoproteins."

Step-by-step diagnostics for disorders of the fat metabolism

"The analysis of blood lipids such as triglycerides, total cholesterol as well as LDL and HDL cholesterol using enzymatic methods will also in future play a key role in the analysis of the lipid metabolism," says Plonné. However, if the baseline lipid levels are in a border area or somewhat inconspicuous in high-risk patients, extended lipoprotein diagnostics can help physicians to better assess health risks and adapt treatment to a particular patient.

In Germany, patients still have to pay for blood lipid analyses using NMR spectroscopy out of their own pockets, while the cost of density gradient ultracentrifugation is already covered by health insurance. What is missing at the moment is larger clinical studies to confirm that measuring and reducing the quantity of small dense LDL particles results in fewer heart attacks, strokes and deaths compared to currently used LDL measurements. "Atherosclerosis trials take decades, and the trials that provide the basis for medical guidelines and recommendations do not even take into account the different lipoprotein subclasses," says Plonné. At any rate, Plonné is convinced that "it is less the cholesterol itself, and more the cholesterol-containing particles that are to blame for atherosclerosis."

Article

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Further information

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