Dysfunctional high-density lipoprotein: not only quantity but first of all quality?

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According to many studies, low levels of high-density lipoprotein cholesterol (HDL-C) are an independent risk factor for coronary artery disease [1]. HDL has several pleiotropic properties apart from reverse cholesterol transport; these include anti-oxidant, anti-inflammatory, anti-infectious, anti-proliferative, antithrombotic and vasodilator actions [2–4].

Randomised controlled trials, prospective and genetic studies, as well as meta-analyses have produced controversial results regarding treating low HDL-C levels [5, 6].

The functionality of HDL-C, as well as the role of dysfunctional HDL (dysHDL) in the prediction of cardiovascular (CV) risk has generated considerable debate. Therefore, we read with interest the Dodani *et al.* study [7] which showed that dysHDL was significantly associated ($p = 0.0024$) with common carotid artery intima-media thickness (CCA-IMT) in 129 South Asian immigrants. Chronic inflammation transforms HDL to dysHDL [4]. However, the authors did not mention any correlation between high sensitivity C-reactive protein levels and the quantity of dysHDL or whether routinely measured HDL-C levels correlated with CCA-IMT and if any such relationship differs from dysHDL.

It is apparent from the above, that not only the quantity, but also the quality of HDL matters (*Quantity and Quality; "Q and Q"*). As a result, there is a need for new drugs that, apart from raising HDL-C levels, can improve HDL function [8, 9]. Cholesterol ester transfer protein (CETP) inhibitors (anacetrapib and evacetrapib) seem to be promising [6]. However, there is no class effect, as the development of other CETP inhibitors (torcetrapib and dalcetrapib) was discontinued [6].

It is worth emphasizing that we are at the beginning of dysHDL research. Some issues need to be considered before confirming the potential predictive role of dysHDL [4]. We need an easy and direct diagnostic method for dysHDL evaluation (possibly *via* measurement of highly specific microRNAs (miRs), as suggested in the DYS-HDL trial), as well as an optimal method for HDL subfraction analysis (to establish if certain subfractions are dysfunctional) [2, 10, 11].

HDL carries specific miRs [10, 11]. Therefore, dysHDL-miRs, as well as HDL subfraction-miRs, could prove to be novel biomarkers of CV disease [10, 11]. Targeting HDL-miRs might also be a promising basis for drug development [10, 11]. It is crucial to identify the patients and conditions at the highest risk of dysHDL formation. This population might benefit most from improving HDL "Q and Q" with a potential subsequent reduction in CV disease residual risk [10–13].

Conflict of interest

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